CUSTOMARY CORRUPTION

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ABSTRACT

For over a hundred years, it has been well-accepted among tort scholars that physicians—as one of the legally recognized professions—determine their own customary practices. Within tort law, and medical malpractice more specifically, customary practice establishes whether physicians breach or uphold the required standard of care toward their patients. The results of our hand-coded examination of decided cases and statutes show a more complex picture. While some states have endeavored to shift the standard away from professional custom, it continues to play a critical, and in many cases a determinative, role in establishing physician liability in most states.

Using illustrative case studies, we demonstrate how this outsized role of customary practice may undermine the ability of tort law to protect patients from harm. Customary practice is shaped by a variety of factors, including physician education, scientific studies, and

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government regulation. Pharmaceutical companies influence these factors to alter physician practices and expand markets for their drugs, often at the expense of patient and public health. This industry pressure directly influences whether a physician is viewed as breaching their legal standard of care, undermining tort law as a form of private regulation of prescribing practices.

To address this problem, this Article argues for a shift in tort doctrine—the explicit abandonment of the rule that customary practice determines breach for prescribing practices, and a move to a reasonableness standard under which professional custom is only one aspect of determining breach. We address the doctrinal and medical benefits of such a shift and conclude that it is essential to the integrity of the private regulation of pharmaceuticals. Our thesis and arguments have significant implications for the role of custom in medicine more generally and for other legally recognized professions.

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INTRODUCTION

> The well-nigh universal rule in this country is that a physician will not be liable for negligence in a medical malpractice case unless he fails "to possess and employ such reasonable skill and care as are commonly had and exercised by reputable, average physicians in the same general system or school of practice...." Under this rule, the medical profession is able to establish its own standard of care. Thus, it is medical custom, rather than standards of reasonableness determined by judges and juries, against which the conduct of a physician is measured.[1]

Physicians and other health care providers apply their knowledge and expertise to determine appropriate treatments for their patients.[2] In the context of prescription drugs, this role extends to decisions about when to prescribe drugs for both Food and Drug Administration (FDA) approved (on-label) and non-FDA approved (off-label) uses.[3] This results in prescribers playing an important role in the U.S. medical system and economy. The proportion of Americans taking at least one prescription drug on- or off-label is around 50 percent, with 12.8 percent taking five or more; in 2020, this amounted to an estimated 6.32 billion prescriptions.[4] Pharmaceutical costs are the third-highest driver of health care spending after hospital and physician services, an estimated $449.7 billion in 2023 (with one study estimating expenses as high as $535.3 billion in 2021).[5]

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1. Richard N. Pearson, *The Role of Custom in Medical Malpractice Cases*, 51 IND. L.J. 528, 528 (1976) (footnote omitted) (citing JOHN R. WALTZ & FRED E. INBAU, MEDICAL JURISPRUDENCE 42 (1971)).

2. By "physicians" we mean physicians, other health care providers with prescribing authority, and their medical agents. This may include advanced practice nurses, physician assistants, and other supervised medical practitioners.

3. *See Understanding Unapproved Use of Approved Drugs "Off Label,"* FDA (Feb. 5, 2018), https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/understanding-unapproved-use-approved-drugs-label [https://perma.cc/YW5J-VM7M].

4. *Therapeutic Drug Use*, CDC (Nov. 3, 2023), https://www.cdc.gov/nchs/fastats/drug-use-therapeutic.htm [https://perma.cc/559B-FVHC]; Matej Mikulic, *Total Number of Medical Prescriptions Dispensed in the U.S. from 2009 to 2022*, STATISTA (May 22, 2024), https://www.statista.com/statistics/238702/us-total-medical-prescriptions-issued/ [https://perma.cc/4ACJ-75A8].

5. *National Health Expenditures 2023 Highlights*, CTRS. FOR MEDICARE & MEDICAID

Pharmaceutical companies have long recognized the important role physicians and other prescribers play in determining whether, when, and how to prescribe drugs to their patients.[6] While the FDA serves as the initial gatekeeper of drug use by determining whether a drug is safe and effective for a particular disease and the method of treatment, once the drug is on the market, physicians and other prescribers may use it beyond its approved indications.[7] Indeed, off-label prescribing of prescription drugs is frequent, particularly for children and older people,[8] even in situations where clinical efficacy is lacking, and there are significant concerns about proper dosing and safety.[9]

Recognizing the pivotal role of prescribers (and increasingly also payors or funders of health care) in the pharmaceutical marketplace, pharmaceutical companies spend billions of dollars cultivating relationships with physicians,[10] other medical professionals with

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SERVS., https://www.cms.gov/files/document/highlights.pdf [https://perma.cc/WMC2-D53N]; Eric M. Tichy, James M. Hoffman, Katie J. Suda, Matthew H. Rim, Mina Tadrous, Sandra Cuellar, John S. Clark, Michelle D. Wiest, Linda M. Matusiak & Glen T. Schumock, *National Trends in Prescription Drug Expenditures and Projections for 2021*, 78 AM. J. HEALTH-SYST. PHARMACY 1294, 1296 tbl.1 (2021).

6. *See, e.g.*, Jeremy A. Greene & Scott H. Podolsky, *Keeping Modern in Medicine: Pharmaceutical Promotion and Physician Education in Postwar America*, 83 BULL. HIST. MED. 331 (2009) (exploring the role of the pharmaceutical industry in medical education and prescribing practices over time).

7. *Understanding Unapproved Use of Approved Drugs "Off Label"*, *supra* note 3.

8. Divya Hoon, Matthew Taylor, Pooja Kapadia, Tobias Gerhard, Brian L. Strom & Daniel B. Horton, *Trends in Off-Label Drug Use in Ambulatory Settings: 2006-2015*, PEDIATRICS, Oct. 2019, at 91; Christopher M. Wittich, Christopher M. Burkle & William L. Lanier, *Ten Common Questions (and Their Answers) About Off-Label Drug Use*, 87 MAYO CLINIC PROC. 982, 983 (2012).

9. HASSAN Z. SHEIKH, CONG. RSCH. SERV., R45792, OFF-LABEL USE OF PRESCRIPTION DRUGS 4 (2021); Katelyn Yackey & Rachel Stanley, Commentary, *Off-Label Prescribing in Children Remains High: A Call for Prioritized Research*, PEDIATRICS, Oct. 2019, at 101, 101.

10. *See, e.g.*, Aaron Mitchell & Deborah Korenstein, *Drug Companies' Payments and Gifts Affect Physicians' Prescribing. It's Time to Turn off the Spigot*, STAT (Dec. 4, 2020), https://www.statnews.com/2020/12/04/drug-companies-payments-gifts-affect-physician-prescribing/ [https://perma.cc/GQ7M-YUL4]; Hannah Fresques, *Doctors Prescribe More of a Drug if They Receive Money from a Pharma Company Tied to It*, PROPUBLICA: DOLLARS FOR DOCTORS (Dec. 20, 2019, 12:00 PM), https://www.propublica.org/article/doctors-prescribe-more-of-a-drug-if-they-receive-money-from-a-pharma-company-tied-to-it [https://perma.cc/WJG4-EZCE]; *see also* Alix Spiegel, *How to Win Doctors and Influence Prescriptions*, NPR: DOLLARS FOR DOCS: HOW PHARMA MONEY INFLUENCES PHYSICIAN PRESCRIPTIONS (Oct. 21, 2010, 4:11 PM), https://www.npr.org/series/130598927/dollars-for-docs-how-pharma-money-influences-physician-prescriptions [https://perma.cc/MH7J-GD7R]; Charles Ornstein, Tracy Weber &

prescribing authority, medical associations, patient groups,[11] co-pay foundations,[12] long-term care pharmacies,[13] and many other actors who directly or indirectly influence prescribing practices.[14] Physicians and other medical professionals then serve as spokespeople, authors of scientific articles, medical educators, and other supporters of particular drugs.[15] The momentum for a drug's expanded use may be so great that new markets are created for uses of drugs that previously had not been part of medical practice. When this happens, the customary practice of prescribing drugs, and the behavior required to meet the tort standard for patient care, may shift. One of the most salient examples of such a shift was the pressure exerted by opioid manufacturers like Purdue Pharma to encourage prescriptions of opioids, formerly reserved for acute pain and

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Ryann Grochowski Jones, *We Found Over 700 Doctors Who Were Paid More than a Million Dollars by Drug and Medical Device Companies*, PROPUBLICA: DOLLARS FOR DOCTORS (Oct. 17, 2019, 12:00 PM), https://www.propublica.org/article/we-found-over-700-doctors-who-were-paid-more-than-a-million-dollars-by-drug-and-medical-device-companies [https://perma.cc/67V7-ZMKJ].

11. *See, e.g.*, Emily Kopp, Sydney Lupkin & Elizabeth Lucas, *Drug Companies Paid $116 Million to Patient Advocacy Groups in 2015 Alone, New Data Suggests*, PBS NEWS (Apr. 6, 2018, 11:12 AM), https://www.pbs.org/newshour/health/drug-companies-pay-116-million-to-patient-advocacy-groups-in-2015-alone-new-data-suggests [https://perma.cc/755Y-Y5SN].

12. Press Release, U.S. Att'y's Off. Dist. of Mass., Biogen Agrees to Pay $22 Million to Resolve Allegations that It Paid Kickbacks Through Two Co-Pay Foundations (Dec. 17, 2020), https://www.justice.gov/usao-ma/pr/biogen-agrees-pay-22-million-resolve-allegations-it-paid-kickbacks-through-two-co-pay [https://perma.cc/Z5K8-CNWF].

13. *See, e.g.*, James McNair, *Louisville-Based PharMerica Settles Fraud Lawsuit*, LOUISVILLE PUB. MEDIA (Jan. 5, 2016, 7:07 PM), https://www.lpm.org/2016-01-05/louisville-based-pharmerica-settles-fraud-lawsuit [https://perma.cc/B4WV-YKTA].

14. *See, e.g.*, Rachana Pradhan, *Millions of Dollars Flow from Pharma to Patient Advocacy Groups*, KFF HEALTH NEWS (Dec. 15, 2023), https://kffhealthnews.org/news/article/health-202-pharma-money-patient-advocacy-groups-public-citizen/ [https://perma.cc/H8GF-9DD6]; Charles Ornstein, *Transparency Program Obscures Pharma Payments to Nurses, Physician Assistants*, PROPUBLICA: DOLLARS FOR DOCTORS (July 6, 2015, 10:00 AM), https://www.propublica.org/article/transparency-program-obscures-pharma-payments-nurses-physician-assistants [https://perma.cc/L652-U5GX].

15. *See, e.g.*, Sunita Sah & Adriane Fugh-Berman, *Physicians Under the Influence: Social Psychology and Industry Marketing Strategies*, 41 J.L. MED. & ETHICS, 665, 665-66 (2013); Joel Lexchin & Adriane Fugh-Berman, *A Ray of Sunshine: Transparency in Physician-Industry Relationships Is Not Enough*, 36 J. GEN. INTERNAL MED. 3194, 3194-95 (2021); Eric G. Campbell, *Doctors and Drug Companies—Scrutinizing Influential Relationships*, 357 NEW ENG. J. MED. 1796, 1796 (2007); Adriane Fugh-Berman & Douglas Melnick, *Off-Label Promotion, On-Target Sales*, 5 PLOS MED. 1432, 1433-34 (Oct. 28, 2008), https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0050210 [https://perma.cc/N6JP-MZZG].

terminal cancer diagnoses, for the general treatment of chronic pain.[16]

In response to some of the most obvious and direct conflicts of interest that relationships between companies—including pharmaceutical companies—and physicians and other supporting professionals can create, Congress enacted a series of patient protection laws. The Medicare and Medicaid Fraud and Abuse Statute, commonly known as the Anti-Kickback Statute, bars monetary inducements for referrals or product use payable by federal health care programs.[17] The Physician Payments Sunshine Act (Section 6002 of the Affordable Care Act) requires pharmaceutical and other companies to report payments made to physicians or their designees.[18] Further, recognizing that the federal and state False Claims Acts (FCAs) have been used in litigation against drug and device manufacturers marketing off-label uses or providing physicians inducements,[19] Congress incorporated language into the Affordable Care Act confirming that violations of the Anti-Kickback Statute are per se violations of the False Claims Act.[20]

While these statutes mitigate some of the ways in which pharmaceutical companies may unduly influence physician practices, they fail to address the broader effects of industry influence on professional custom. Physicians may be fully compliant with these laws—for example, they may not receive remuneration or other inducements—and still alter their treatment decisions due to corporate influence. Indeed, physicians may not be aware of corporate influence in establishing markets and customs for drug use through corporate sponsored continuing medical education programs, journal articles, or physician spokespersons on social

16. *See, e.g.*, Liza Vertinsky, *Pharmaceutical (Re)Capture*, 20 YALE J. HEALTH POL'Y L. & ETHICS 146, 188-89, 191 (2021).

17. 42 U.S.C. § 1320a-7b(b).

18. Physician Payments Sunshine Act § 6002, 42 U.S.C. § 1320a-7h(a).

19. *See, e.g.*, United States *ex rel.* Brown v. Celgene Corp., No. CV 10-3165, 2014 U.S. Dist. LEXIS 99815, at *12-14 (C.D. Cal. July 10, 2014) (finding off-label uses must be supported by compendia, which are private publications identified by the government as sources to determine medical necessity for reimbursement).

20. 42 U.S.C. § 1320a-7b(g) ("[A] claim that includes items or services resulting from a violation of [the Anti-Kickback Statute] constitutes a false or fraudulent claim for purposes of subchapter III of chapter 37 of title 31 [the False Claims Act].").

media.[21] Moreover, even if illegal conduct that influences prescribing practices is discovered and punished, this may not reset the distorted prescribing practices that have been normalized as customary practices.

The implications of this hidden vulnerability in tort law are profound. Once prescribing a drug becomes routine, customary practice is redefined; that is, the legal standard for malpractice (a tort that sounds in negligence) changes. This is because professional custom in medical malpractice is understood to be what is routine or standard "under similar conditions and like surrounding circumstances,"[22] or in "the medical profession generally."[23] Put differently, it conforms with medical industry norms.[24] And unlike most other occupations—that is, those that do not fall within the small set of legally recognized professions[25]—in medicine, professional custom generally has determined whether a physician has met or breached their legal standard of care for a century.[26]

Professional custom thus serves as a sword and a shield[27]: physicians are in legal breach if they do not follow professional custom and are likely shielded from legal liability if they do.[28] By exploiting the role of custom as a sword, corporate influence over professional custom can impose legal liability on physicians if they

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21. *See* Carl Elliott, *Relationships Between Physicians and Pharma: Why Physicians Should Not Accept Money from the Pharmaceutical Industry*, 4 NEUROLOGY CLINICAL PRAC. 164, 164, 166 (2014); *see also* Ritika Goel, *Why Do Doctors Still Think Pharma Doesn't Influence Them?*, HEALTHY DEBATE (Apr. 8, 2013), https://healthydebate.ca/2013/04/about-healthy-debate/opinions-about-healthy-debate/why-do-doctors-still-think-pharma-doesnt-influence-them/ [https://perma.cc/FVE4-N8WA]; Sah & Fugh-Berman, *supra* note 15, at 668-70.

22. Johnson v. Myers, 165 S.E.2d 739, 742 (Ga. Ct. App. 1968).

23. McNabb v. Landis, 479 S.E.2d 194, 196 (Ga. Ct. App. 1996).

24. *See* Richard A. Epstein, *Customary Practices and the Law of Torts*, *in* THE NEW PALGRAVE DICTIONARY OF ECONOMICS AND THE LAW 579, 582 (Peter Newman ed., 1998) (citing Clarence Morris, *Custom and Negligence*, 42 COLUM. L. REV. 1147 (1942)).

25. This narrow subset of professions includes doctors, lawyers, and accountants.

26. *See* RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYS. & EMOT. HARM § 13 cmt. b (AM. L. INST. 2010).

27. Kenneth S. Abraham, *Custom, Noncustomary Practice, and Negligence*, 109 COLUM. L. REV. 1784, 1786 (2009).

28. *See* RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYS. & EMOT. HARM § 13 reporter's note on cmt. b (AM. L. INST. 2010) ("In negligence claims against professionals, the standard of reasonable care is commonly determined by professional custom. Thus, the defendant who complies with custom is for that reason free of negligence, while the defendant who departs from custom can for that reason alone be found negligent.").

fail to follow a custom, even if they believe it is harmful or ineffective. By exploiting the role of professional custom as a shield, corporate influence can shape prescribing practices by limiting liability risk for prescribers if they act in concert with each other.

When industry incentive does not correlate with public or individual patient health, the impact can be deadly. Patients may be harmed or even die as inappropriate drugs are prescribed. Health care payors—private and public—may be saddled with even higher costs. And perhaps most importantly from a legal standpoint, the compensatory and deterrent functions of tort law to protect patients are eviscerated when corporate-driven standards disrupt, and even drive, the practice of medicine. The ability of industry to influence standards of care significantly impedes private litigation, which is arguably the last check on an acceptable standard of care.[29]

This Article argues for a major shift in tort doctrine to address this distortion of law; namely, that the professional custom standard in medicine should be explicitly replaced with a reasonableness inquiry.[30] As a result of this shift, evidence of professional custom alone would not determine whether the reasonable standard of care has been met in negligent prescribing litigation. Moreover, evidence of industry influence over prescribing practices might be admissible to determine the reasonableness of care. This shift is the best way to restore the form and function of tort law and to bring order to existing judicial practices across states.

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29. State licensing laws and certain federal laws, such as the Controlled Substances Act, also govern prescribing practices, though they are under attack. *See, e.g.*, Andrew Chung & John Kruzel, *Federal Agency Powers in the Crosshairs at the US Supreme Court*, REUTERS (July 5, 2023, 2:08 PM), https://www.reuters.com/legal/federal-agency-powers-crosshairs-us-supreme-court-2023-07-04/ [https://perma.cc/WRZ3-7SP3]; Andrea Scoseria Katz & Noah A. Rosenblum, *Becoming the Administrator-in-Chief:* Myers *and the Progressive Presidency*, 123 COLUM. L. REV. 2153, 2155, 2169 (2023) (discussing and critiquing the Supreme Court's current assault on the administrative state in recent influential cases). Additionally, public health authorities, which may affect the delivery of health care, have been weakened by recent appellate and Supreme Court decisions, making the role of tort law as a source of patient protection even more important. *See* Lauren Weber & Joel Achenbach, *Covid Backlash Hobbles Public Health and Future Pandemic Response*, WASH. POST (Mar. 8, 2023, 6:00 AM), https://www.washingtonpost.com/health/2023/03/08/covid-public-health-backlash/ [https://perma.cc/5ZHK-MDZC]. On the sustainability of public and private enforcement, see Gary S. Becker & George J. Stigler, *Law Enforcement, Malfeasance, and Compensation of Enforcers*, 3 J. LEGAL. STUD. 1, 13-16 (1974).

30. *See, e.g.*, Philip G. Peters, Jr., *The Quiet Demise of Deference to Custom: Malpractice Law at the Millennium*, 57 WASH. & LEE L. REV. 163, 201, 204 (2000).

To support this thesis, the Article proceeds in several steps. Part I interrogates the relatively unquestioned role of professional custom in medical malpractice among legal scholars. It begins by describing the historical role of custom in medical malpractice generally and then with respect to prescribing for both on- and off-label drug uses. Next, it presents our empirical survey findings of decided cases and statutes to show a complex and muddled picture of customary practice in which it persists as an important factor, even when states try to move away from it. Our survey shows that while fewer than half the states with a clear doctrinal practice have a professional custom standard, professional custom plays an outsized role in states where the standard is unclear, as well as in half the states that have shifted to a reasonableness inquiry. This means that professional custom remains a critical part of judicial decision-making in up to three-fourths of states.

Part II uses three case studies to illustrate some of the ways in which allowing customary practice to determine breach in medical malpractice could undermine the ability of tort law to protect patients from harm. We show how customary practice, which is shaped by a variety of factors, including physician education, scientific studies, and government regulation, is susceptible to industry influence. By influencing customary practice, industry is effectively shaping when physicians meet the legal standard of care, undermining tort law as a form of private regulation of prescribing practices.

Part III outlines legal and medical arguments for abandoning professional custom for prescribing practices and moving toward a reasonableness inquiry. It also addresses long-standing counter-arguments to this shift, showing that, in fact, a reasonableness standard better addresses the concerns traditionally raised. The Article concludes by discussing the implications of our doctrinal proposal for medical malpractice generally, as well as for the other legally recognized professions.

I. PROFESSIONAL CUSTOM AND STANDARD OF CARE IN TORT

This Part describes the role that professional custom plays in tort liability for physicians and industry influence over that custom. It first discusses how historically physicians established their own

customs of reasonable practice in medicine as part of a legally recognized profession. Next, it examines custom in prescribing practices specifically, including the role and limits of the required drug approval process in determining custom. Last, this Part presents the results of an empirical study about professional custom, indicating that while some states have rejected custom as determinative, the standard continues to play a dominant role in the majority of states and is inconsistently applied.

A. Overview of Professional Custom in Medical Malpractice

1. Role of Custom

Negligence law is based on the idea that individuals owe each other a reasonable standard of care in their interactions. This obligation imposes a duty on individuals to act with reasonable care in each set of circumstances. A duty is breached when a party fails to exercise a reasonable standard of care.[31] In medicine, this is interpreted to mean that a physician must act reasonably for someone in their profession, and, more specifically, someone in their medical specialty.[32] A physician is responsible for medical malpractice when they breach a duty of care that actually and proximately causes an injury.[33]

Custom is one tool to establish breach in negligence.[34] "Custom" is understood in law generally to mean "[a] usage or practice of the people, which, by common adoption and acquiescence, and by long and unvarying habit, has become compulsory, and has acquired the force of a law with respect to the place or subject-matter to which it relates."[35] Accordingly, in tort law—including medical malpractice—custom is often determined by common practice.[36] The well-

31. *See, e.g.*, Daniele Bryden & Ian Storey, *Duty of Care and Medical Negligence*, 11 CONTINUING EDUC. ANAESTHESIA CRITICAL CARE & PAIN, 124, 124 (2011).

32. *See* B. Sonny Bal, *An Introduction to Medical Malpractice in the United States*, 467 CLINICAL ORTHOPAEDICS & RELATED RSCH. 339, 342 (2008).

33. *Id.*

34. Other tools include cost-benefit analysis, negligence per se, and the use of the evidentiary doctrine res ipsa loquitur to infer breach in certain circumstances.

35. *Custom*, BLACK'S LAW DICTIONARY (4th rev. ed. 1968).

36. DAN B. DOBBS, PAUL T. HAYDEN & ELLEN M. BUBLICK, THE LAW OF TORTS § 292 (2d ed. 2024).

known Dobbs treatise on torts, for example, states that "the 'standard' in medical cases is conceived of as the specific procedure or medical conduct that the relevant medical community considered to be acceptable at the time of the alleged negligence."[37]

Medical and other custom is defined by current professional practice within a particular geographic area. Historically, customary practice was established within each locality.[38] Over time, customary practice shifted toward a national standard.[39] Although some courts still look to local practice in determining professional custom, for the most part, when professional custom is used to determine breach, it effectively establishes a national standard of care for a physician in like circumstances.[40]

In most tort cases, custom is evidence of reasonableness for a jury to consider.[41] Therefore, an industry's custom or common practice may be viewed as either reasonable or unreasonable by the jury.[42] If the practice is considered unreasonable, an actor may be found liable for following it. In the oft-cited case, *The T.J. Hooper*, for example, Judge Learned Hand stated that "in most cases reasonable prudence is in fact common prudence; but strictly it is never its measure; [an industry] may have unduly lagged in the adoption of new and available devices."[43]

Meanwhile, for certain legally recognized professions, custom historically determined breach.[44] These professions are the "learned"

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37. *Id.*

38. Orcutt v. Miller, 595 P.2d 1191, 1194 (Nev. 1979) ("[T]he strict locality rule is based on the rationale that there exists gross inequality between physicians practicing in large urban areas and those practicing in more remote rural communities.... [T]he rule ... prevent[s] the small town practitioner from being held to the standard of practice of the more sophisticated urban areas.").

39. *See, e.g.*, Peter Moffett & Gregory Moore, *The Standard of Care: Legal History and Definitions: The Bad and Good News*, 12 W.J. EMERGENCY MED. 109, 110 (2011).

40. Leonard J. Nelson, III, *Medical Malpractice and the Transformation in Health Care Delivery*, 17 CUMB. L. REV. 313, 321 (1987).

41. *See The T.J. Hooper*, 60 F.2d 737, 740 (2d Cir. 1932).

42. *See id.*

43. *Id.*

44. *See, e.g.*, Bryden & Storey, *supra* note 31, at 125 ("In *Crawford v. Board of Governors of Charing Cross Hospital*, a patient sustained a brachial plexus injury from being in one position for too long a time period. An article describing such a complication had been published 6 months previously. However, the anaesthetist had not read this article and was not aware of its implications and so was found not to have breached their duty of care to the patient." (footnote omitted)).

ones and include physicians, lawyers, and accountants.[45] For these professions, custom determines whether a professional acted reasonably or engaged in malpractice. If such a professional fails to follow a custom, they are in breach of a duty to provide reasonable care, and, if they follow it, they are generally shielded from liability.[46]

Because professional custom in medical malpractice establishes what is reasonable, it often is equated with the professional standard of care. But "professional custom" and "standard of care" are not synonymous and are frequently confused by practitioners and courts alike. "Standard of care" is the level of care owed by an actor.[47] This level of care may be one of reasonableness (most common)[48] or impose a duty of extraordinary care. Common carriers, which typically are commercial vehicles that transport a large number of people (such as airplanes, trains, and buses), have a duty of extraordinary care.[49] In medical malpractice, the standard of care is that of a reasonable physician.[50]

"Professional custom," on the other hand, is one tool for establishing reasonableness.[51] So professional custom may inform the standard of care, but it does not alter the level of care owed. This is significant for two reasons. First, despite common misperception, physicians have an ordinary duty of reasonable care for patients, not a heightened or extraordinary duty of care. Second, eliminating the professional custom standard would not alter the standard of care of reasonableness, only the weight evidence of professional custom is given in determining what is reasonable. Adopting a reasonableness rather than a professional custom approach to breach would mean that evidence of professional custom would be relevant but not determinative of breach.[52]

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45. *See* Litchfield v. KPMG, LLP, 285 P.3d 172, 176 & n.18 (Wash. Ct. App. 2012); Goldfarb v. Virginia State Bar, 421 U.S. 773, 779-80 (1975), *abrogated on other grounds by* S. Motor Carriers Rate Conf. Inc. v. United States, 471 U.S. 48 (1985).

46. *See* RESTATEMENT (THIRD) OF TORTS: LIAB. FOR PHYS. & EMOT. HARM § 13 reporter's note on cmt. b (AM. L. INST. 2010).

47. *See Standard of Care*, CORNELL L. SCH. LEGAL INFO. INST., https://www.law.cornell.edu/wex/standard_of_care [https://perma.cc/H46Y-EQ4Z].

48. *Id.*

49. Cox v. Evansville Police Dep't, 107 N.E.3d 453, 465-66 (Ind. 2018).

50. *See* Bryden & Storey, *supra* note 31, at 125.

51. *See* Promen v. Ward, 591 N.E.2d 813, 817 (Ohio Ct. App. 1990).

52. *See id.*

2. Historical Justifications

The historical justifications for deference to physicians to establish their own legally binding standards for professional practice are unclear and rarely discussed in the legal literature. One treatise suggests courts were concerned about reducing "defensive medicine" and controlling health care costs presumably by reducing litigation or litigation risks,[53] but that suggestion is unsubstantiated by case law. One commentator argues without legal support that physicians privilege and their "preferred status" was one justification.[54] Another author suggests that the professional custom standard held physicians accountable to their peers for their actions.[55] Under this rationale, professional custom may have prevailed because physicians were perceived as operating independently of external influence and to the benefit of their patients.[56]

In contrast to rationales finding something unique about the practice of medicine, Theodore Silver suggests that professional custom in medicine may have evolved essentially by judicial accident. Silver argues professional custom resulted from erroneous judicial equation of "standard of care" with "custom."[57] He argues, for example, that early treatises and judicial opinions refer to a "prudent practitioner" rather than a "reasonable person" standard,[58]

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53. *See* 3 FOWLER V. HARPER, FLEMING JAMES, JR. & OSCAR S. GRAY, THE LAW OF TORTS § 17.3, at 583-84 n.6 (2d ed. 1986) ("Another reason for distinguishing at least medical malpractice cases from normal negligence may be that there can be in this field certain unusual consequences of any tendency to reach erroneous determinations of fault. To the extent that such a tendency encourages 'defensive medicine,' it may lead to harm to patients ... and to unusually great economic harm to the public (e.g., through the inflation of medical costs because of unnecessary tests).").

54. *See* Theodore Silver, *One Hundred Years of Harmful Error: The Historical Jurisprudence of Medical Malpractice*, 1992 WIS. L. REV. 1193, 1215 n.67 (discussing Allan H. McCoid, *The Care Required of Medical Practitioners*, 12 VAND. L. REV. 549, 608 (1959)).

55. *See* Pearson, *supra* note 1, at 535-36 (citing McCoid, *supra* note 54).

56. *See id.* at 537 ("[M]edical custom may be accepted as the standard of care in medical malpractice cases because physicians have been thought of as not exploiting the market for medical services for their own gain at the expense of the health of their patients. There is no need for courts to act as a source of pressure to compel the medical profession to give adequate consideration to patient safety and well-being, since the forces that operate within the profession make such extra-professional pressure unnecessary.").

57. Silver, *supra* note 54, at 1193-94, 1222-25.

58. *Id.* at 1224 n.102 ("To render a doctor of medicine liable for negligence, there must ... appear to have been a failure to exercise such diligence or skill as a prudent practitioner of

making it seem semantically that physicians are to determine their own customs.[59]

Indeed, early opinions seem to establish professional custom without precedent or other justification. In 1860, the *Ritchey v. West* court stated for the first time, and without explanation, that a physician was required to "possess and exercise that degree of skill which is ordinarily possessed by members of the profession."[60] Sixteen years later, the court in *Hathorn v. Richmond* reached a similar conclusion, holding that "*ordinary skill* ... means, such skill as doctors ... ordinarily have and exercise in like cases .... If he exercises such skill, then he is not liable."[61] Silver argues *Hathorn* "was much cited at the end of the nineteenth century and at the beginning of the twentieth. During those years, for want of judicial watchfulness, the professional custom rule became entrenched."[62]

Even if professional custom was established by judicial accident, our research indicates that it may have taken hold and prevailed due to concerns about juror (and even judicial) incompetence. Several early cases discuss the inability of laypeople and non-physicians to determine what is reasonable in a case involving alleged medical malpractice and the need for physician expert testimony to guide the jury.[63] Further, most of these early medical malpractice cases assume without discussion that testimony about custom should be dispositive.[64] For example, in 1915, the Supreme Court of Iowa in *Evans v. Roberts* held that "a layman can have no knowledge whether the proper medicine was administered or the proper surgical treatment was given. Whether a surgical operation

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fair ability would have exercised under the same circumstances." (alteration in original) (quoting MELVILLE M. BIGELOW, THE LAW OF TORTS 127 (8th ed. 1907))); *see also* Hathorn v. Richmond, 48 Vt. 557, 558-59 (1876); Ritchey v. West, 23 Ill. 329, 329-30 (1860).

59. Silver, *supra* note 54, at 1224 n.102; *see also* Pearson, *supra* note 1, at 528.

60. 23 Ill. at 329.

61. 48 Vt. at 559.

62. Silver, *supra* note 54, at 1225 (footnote omitted).

63. *See infra* notes 64-68 and accompanying text.

64. *See, e.g.*, Engelking v. Carlson, 88 P.2d 695, 697 (Cal. 1939) ("[W]hen the matter in issue is one within the knowledge of experts only and is not within the common knowledge of laymen, the expert evidence is conclusive."). *But see* Darling v. Charleston Cmty. Mem'l Hosp., 211 N.E.2d 253, 257 (Ill. 1965) ("By the great weight of modern American authority a custom either to take or to omit a precaution is generally admissible as bearing on what is proper conduct under the circumstances, but is not conclusive." (quoting 2 FOWLER V. HARPER & FLEMING JAMES, JR., THE LAW OF TORTS § 17.3, at 977-78 (1956))).

was unskillfully or skillfully performed is a scientific question."[65] Similarly, in *Person v. Lilliendahl*, the Supreme Court of Connecticut found that when faced with "questions beyond the ordinary field of experience of laymen" juries must rely on expert testimony about whether the standard of care is met.[66] Otherwise, as another court noted, "juries [would] be cast into a river of doubt and must establish an arbitrary standard of their own founded upon conjecture and surmise in their effort to reach certain and sure ground."[67] Without scientific and medical education, juries might focus on a plaintiff's harm rather than whether a duty has been breached.[68]

Regardless of the historical explanation for the rise and perseverance of professional custom, and despite the absence of a compelling reason to support its continued use, it has dictated judicial outcomes for over a hundred years.[69] In Part III we argue that prior rationales from law and medicine do not support the continued use of professional custom to determine breach. In fact, a reasonableness standard best addresses some of the concerns that may have motivated the adoption of professional custom as dispositive in medical malpractice, turning the rationales on their head.

3. Tort as Private Regulation of the Practice of Medicine

Prior to leaving this overview, it is important to underscore the role that tort law serves as a form of private regulation of the practice of medicine. Tort law allows injured patients to sue physicians and the institutions they serve to recover compensation for private losses.[70] This differs from the actions of state boards of medicine,

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65. 154 N.W. 923, 926 (Iowa 1915) (quoting Wharten v. Warner, 135 P. 235, 237 (Wash. 1913)).

66. 172 A. 94, 94 (Conn. 1934) (per curiam).

67. Pedigo v. Roseberry, 102 S.W.2d 600, 607 (Mo. 1937).

68. *See* Capolupo v. Wills, 163 A. 454, 455 (Conn. 1932) ("In actions for malpractice against a physician or surgeon, the main issue of the defendant's use of suitable professional skill is generally a topic calling for expert testimony only; also that the plaintiff in such an action often prefers to rest his case on the mere facts of his sufferings, and to rely on the jury's untutored sympathies, without attempting specifically to evidence the defendant's unskillfulness as the cause of those sufferings." (quoting Slimak v. Foster, 138 A. 153, 154 (Conn. 1927))).

69. *See* Silver, *supra* note 54, at 1193-94, 1211.

70. *See* Bal, *supra* note 32, at 346.

which may impose sanctions on physicians but do not compensate injured patients.[71] In the prescribing realm, patients also may sue drug companies as individuals or as part of class actions based on theories of product liability. But, in many of these cases, drug companies are shielded by physician prescribing of the drug.[72] Thus, medical malpractice actions play an important role in safeguarding patients from harmful prescribing practices. But if professional custom standards in law are influenced by corporations, the independent role of law and the ability of patients to recover in tort are undermined. Without addressing corporate influence on professional custom, the practice of medicine and the form and function of tort law as a source of private regulation of prescribing practices will be disrupted and patient care undermined.

B. Professional Custom and Standard of Care in Prescribing Drugs

Although professional custom plays the same role in drug prescribing cases as it does in other medical malpractice cases,[73] the FDA requires that special considerations are given to the regulation of drugs.[74] To understand how governmental determination of drug use and warnings may affect professional custom in prescribing, it is necessary to describe some aspects of the FDA approval process and what the FDA does and does not regulate. This Part will explain how the FDA makes the initial determination of whether drugs can be marketed for approved, or "on-label," uses and how the FDA regulates certain aspects of the marketing of these drugs. It

71. *See About Physician Discipline*, FED'N OF STATE MED. BDS., https://www.fsmb.org/u.s.-medical-regulatory-trends-and-actions/guide-to-medical-regulation-in-the-united-states/about-physician-discipline/ [https://perma.cc/KD7Q-YXMP].

72. *See, e.g.*, Julie Steinberg, *Eli Lilly Shakes Off Nearly All Claims in Cialis Stroke Lawsuit*, BLOOMBERG LAW (Dec. 19, 2023, 11:04 AM), https://news.bloomberglaw.com/litigation/eli-lilly-shakes-off-nearly-all-claims-in-cialis-stroke-lawsuit [https://perma.cc/EW4P-EFVD].

73. *See* Huskey v. Ethicon, Inc., No. 2:12-CV-05201, 2015 WL 4944339, at *12 n.13 (S.D. W. Va. Aug. 19, 2015) (quoting 2 DAN B. DOBBS, PAUL T. HAYDEN & ELLEN M. BUBLICK, THE LAW OF TORTS § 292 (2d ed. 2011) for the standard for professional custom in prescribing case), *aff'd*, 848 F.3d 151 (4th Cir. 2017).

74. *See Development & Approval Process*, FDA (Aug. 8, 2022), https://www.fda.gov/drugs/development-approval-process-drugs [https://perma.cc/TVM2-8MLP].

also discusses physicians' use of drugs for treatments unapproved by the FDA, or "off-label" uses.

1. On-Label Use

Under federal law, all new drugs in the United States must be shown to be "safe and effective for their intended use" before they are approved to be marketed.[75] The FDA evaluates new drugs based on information provided by the manufacturer to determine whether the drug is effective for its indicated population and purpose and whether the health benefits of taking the drug outweigh the known risks for its specified use.[76] FDA approval includes determinations of the dose, dose forms, conditions for which the drug is indicated, patient groups for which the drug may be used, and drug label content, as supported by clinical trials.[77] If the FDA approves a drug in this process, it may be marketed for on-label use according to the content of the FDA's approved drug label.[78]

The FDA specifies that drug labels have (1) "a summary of the essential scientific information needed for the safe and effective use of the drug; and [(2)] ... the Prescribing Information [(PI)], FDA-approved patient labeling (Medication Guides, Patient Package Inserts, and/or Instructions for Use), and/or carton and container labeling."[79] The drug manufacturer proposes the label, which the FDA reviews and may revise.[80] Given its role in drafting the PI, the

75. *See Unapproved Drugs*, FDA (May 9, 2024), https://www.fda.gov/drugs/enforcement-activities-fda/unapproved-drugs [https://perma.cc/5U4N-CU9G].

76. *See Development & Approval Process*, *supra* note 74. The FDA approval process includes an "[a]nalysis of the target condition and available treatments," "[a]ssessment of benefits and risks from clinical data," and the availability of "[s]trategies for managing risks." *See id.* (emphasis omitted).

77. *See, e.g.*, AGATA DABROWSKA & SUSAN THAUL, CONG. RSCH. SERV., R41983, HOW FDA APPROVES DRUGS AND REGULATES THEIR SAFETY AND EFFECTIVENESS 4-7, 9 (May 8, 2018).

78. *See Development & Approval Process*, *supra* note 74. Approval may be expedited to address a serious or life-threatening condition for which there are limited or no alternative treatments. *See id.*

79. *FDA's Labeling Resources for Human Prescription Drugs*, FDA (Apr. 4, 2024), https://www.fda.gov/drugs/laws-acts-and-rules/fdas-labeling-resources-human-prescription-drugs [https://perma.cc/8WNR-P487].

80. *Frequently Asked Questions About Labeling for Prescription Medicines*, FDA (Apr. 1, 2024), https://www.fda.gov/drugs/fdas-labeling-resources-human-prescription-drugs/frequently-asked-questions-about-labeling-prescription-medicines [https://perma.cc/33J7-35ZB].

manufacturer can strategically include information that lays the foundation for encouraging off-label use.

Drug labels are the primary source of prescribing information for clinicians and, to a limited degree, patients.[81] The full PI includes information about "[b]oxed [w]arning[s]," "[i]ndications and [u]sage," "[d]osage and [a]dministration," "[d]osage [f]orms and [s]trengths," "[c]ontraindications," "[w]arnings and [p]recautions," "[a]dverse [r]eactions," "[d]rug [i]nteractions," "[u]se in [s]pecific [p]opulations," "[d]rug [a]buse and [d]ependence," "[o]verdosage," "[d]escription," "[c]linical [p]harmacology," "[n]onclinical [t]oxicology," "[c]linical [s]tudies," "[r]eferences," "[h]ow [s]upplied/[s]torage and [h]andling," and "[p]atient [c]ounseling."[82] This information is made available by the drug manufacturers in a variety of ways, including required electronic access via the FDA website, which uses an interagency online health information clearinghouse called DailyMed,[83] and via print and electronic references such as the Physicians' Desk Reference and subscription service websites.[84]

Drug labeling also includes Patient Package Inserts (PPI), which provide the patient with abbreviated instructions for use.[85] PPIs are largely voluntary; they are mandated only for oral contraceptives and drugs containing estrogen.[86] As a general matter, PPIs do not alert patients to the fact that a drug may be prescribed for uses or in ways outside the FDA indication.[87]

2. Off-Label Use

The FDA does not regulate off-label use, which entails drugs being prescribed for an indication that is not FDA approved.[88] This

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81. *See id.*

82. *Id.*

83. *See The FDA Announces New Prescription Drug Information Format*, FDA (Dec. 4, 2015), https://www.fda.gov/drugs/laws-acts-and-rules/fda-announces-new-prescription-drug-information-format [https://perma.cc/C2A5-AUQH].

84. *See* Joseph P. Nathan & Etty Vider, *The Package Insert*, U.S. PHARMACIST, May 2015, at 8, 9-10.

85. *See Frequently Asked Questions About Labeling for Prescription Medicines*, *supra* note 80.

86. *Id.*

87. *See id.*

88. *See Understanding Unapproved Use of Approved Drugs "Off Label*," *supra* note 3.

is because the FDA does not regulate the practice of medicine[89] or control, with limited exceptions,[90] how doctors prescribe FDA-approved medicines once they are on the market.[91] In general, doctors may legally prescribe FDA-approved drugs for off-label uses when they believe it is in the best interests of their patients.[92] This may include differential dosing or use of an FDA-approved adjunct therapy drug as a monotherapy.[93] The FDA provides only general guidance for off-label use: "If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and sound medical evidence, and to maintain records of the product's use and effects."[94] State law also provides little guidance for off-label drug use, and medical malpractice laws in most states do not even require that a physician disclose that a drug is being used off-label.[95]

The practice of off-label prescribing is common and increasing across medical specialties.[96] According to one commentator, this is

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89. AGATA BODIE, CONG. RSCH. SERV., R45792, OFF-LABEL USE OF PRESCRIPTION DRUGS 1-2 (Feb. 23, 2021).

90. *See, e.g.*, Patricia J. Zettler, *Pharmaceutical Federalism*, 92 IND. L.J. 845, 845 (2017) ("[S]tate regulatory efforts, and the nascent litigation about them, demonstrate that the preemptive reach of the FDA's authority extends into medical practice regulation in some circumstances.").

91. *See* Wendy Teo, *FDA and the Practice of Medicine: Looking at Off-Label Drugs*, 41 SETON HALL LEGIS. J. 305, 305-06 (2017) (describing a deferential stance of the FDA with respect to the practice of medicine, often referred to as the "practice of medicine exception," and the tensions that arise "between the role of [the] FDA in safeguarding the public from unsafe drugs and the autonomy that physicians have in prescribing off-label medication in the practice of medicine" (internal quotation marks omitted)).

92. *See* DABROWSKA & THAUL, *supra* note 77, at 24 ("Despite the indications for use in the approved labeling, a licensed physician may—except in highly regulated circumstances—prescribe the approved drug without restriction. A prescription to an individual whose demographic or medical characteristics differ from those indicated in a drug's FDA-approved labeling is called *off-label use* and is accepted medical practice." (footnote omitted)).

93. *See* SHEIKH, *supra* note 9.

94. *"Off-Label" and Investigational Use of Marketed Drugs, Biologics, and Medical Devices: Guidance for Institutional Review Boards and Clinical Investigators*, FDA (May 6, 2020), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/label-and-investigational-use-marketed-drugs-biologics-and-medical-devices [https://perma.cc/TWY3-HEZ6].

95. *See* Sandra H. Johnson, *Polluting Medical Judgment? False Assumptions in the Pursuit of False Claims Regarding Off-Label Prescribing*, 9 MINN. J.L. SCI. & TECH. 61, 68-69 (2008).

96. Shariful A. Syed, Brigham A. Dixson, Eduardo Constantino & Judith Regan, *The Law*

likely because, in some cases, pharmaceutical companies have an incentive to "seek a narrow approved use ... to minimize the delay to market and reduce the investment in research required to meet FDA standards for approval."[97] Once a drug is approved for one purpose, it can theoretically be used for any purpose.[98] Another author suggests that off-label use is "often considered the standard of care."[99] Indeed, off-label prescribing accounts for an estimated 21 percent of prescriptions by general or family medical practitioners, with higher rates for specialists.[100]

Several factors drive the prescription of drugs off-label. These include a drug's usefulness in an unstudied population (such as use of an adult drug in pediatrics); lack of alternatives to treat a life threatening disease; a drug's usefulness in treating diseases that share medically relevant features to the disease for which the drug was approved; or usefulness of other medications in the same class as an FDA-approved drug that are not approved for that indication.[101] Physicians also may be influenced to prescribe off-label through informal information exchanges among peers on social media and other outlets.[102] As one court noted with respect to off-label uses, drug manufacturers "expect and the custom is that after a material has been available for a period of time, physicians using it rely primarily on their own experience and the published literature of colleagues concerning its use in actual practice."[103]

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and Practice of Off-Label Prescribing and Physician Promotion, 49 J. AM. ACAD. PSYCHIATRY & L. ONLINE 53, 53-54 (2021), https://jaapl.org/content/jaapl/49/1/53.full.pdf [https://perma.cc/55DZ-GQ74].

97. Johnson, *supra* note 95, at 70 (citing Mitchell Oates, *Facilitating Informed Medical Treatment Through Production and Disclosure of Research into Off-Label Uses of Pharmaceuticals*, 80 N.Y.U. L. REV. 1272, 1280 (2005)).

98. *See id.* at 70-71.

99. Danielle Holley, Comment, *Balancing on the Edge: The Implications and Acceptability of Off-Label Drug Use*, 19 ALB. L.J. SCI. & TECH. 633, 634 (2009).

100. *See* Syed et al., *supra* note 96, at 53-54.

101. *See id.* at 55-56 (describing factors that may motivate off-label drug sales).

102. *See* Holley, *supra* note 99, at 638-39 ("[O]ff-label use often does not have the backing of adequate scientific data. Rather, it becomes common practice after there have been scholarly articles by other physicians or researchers. Articles have been written based upon individual consults, or miniature experiments, conducted by physicians as the physician tailors certain drugs to fit the needs of their individual patients without knowledge of potential risks and side-effects. The issue lies in those first-line therapies before the use becomes standard or a commonality." (footnotes omitted)).

103. Salgo v. Leland Stanford Jr. Univ. Bd. of Trs., 317 P.2d 170, 180 (Cal. Dist. Ct. App.

As the case studies in Part II illustrate, the regulatory framework governing prescribing practices leaves open a myriad of opportunities for corporate influence on professional custom. Corporations provide the FDA with the data to assess the efficacy and safety of drugs and their proposed labels.[104] The scope of a label determines on-label use but also creates opportunities to encourage related off-label uses.[105] Once a drug is approved for commercial sale, corporations may market it using paid academic spokespeople, commissioned studies, continuing medical education programs, and a variety of other tools that impact prescribing decisions.[106] The case studies highlight ways in which an exclusive reliance on professional custom to determine reasonable care may undermine the ability of tort law to protect patients.

Before turning to the ways in which industry shapes customary practice, we bridge the gap between tort theory and practice through a survey of the current role of professional custom in determining breach in medical malpractice claims across all fifty states. These data illuminate the current role of professional custom and inform our proposed doctrinal shift in Part III.

C. Survey of Current State Law on Customary Practice

The complexity of the current role of professional custom is not reflected in the legal literature. Many casebooks and treatises, as well as earlier versions of the Restatement of Torts, assume that professional custom determines breach in medical malpractice.[107]

1957).

104. *See Development & Approval Process*, *supra* note 74.

105. *Understanding Unapproved Uses of Approved Drugs "Off Label"*, *supra* note 3.

106. *See* Aaron S. Kesselheim, Michelle M. Mello & David M. Studdert, *Strategies and Practices in Off-Label Marketing of Pharmaceuticals: A Retrospective Analysis of Whistleblower Complaints*, 8 PLOS MED. 5, 6 (Apr. 5, 2011), https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1000431 [https://perma.cc/A2E8-ZHSZ].

107. *See* Silver, *supra* note 54, at 1212 & n.59; *see also* Hall v. Hilbun, 466 So. 2d 856, 860, 868, 871 (Miss. 1985); Hinlicky v. Dreyfuss, 791 N.Y.S.2d 221, 223 (App. Div. 2005), *aff'd*, 848 N.E.2d 1285 (N.Y. 2006). *But see* RESTATEMENT (THIRD) OF TORTS: MED. MALPRACTICE § 5(a) (AM. L. INST., Tentative Draft No. 2, 2024) ("The standard of reasonable medical care is the care, skill, and knowledge regarded as competent among similar medical providers in the same or similar circumstances."); *id.* reporter's note on cmt. c ("Negligence cannot be excused on the grounds that others practice the same kind of negligence." (citing Vassos v. Roussalis, 625 P.2d 768, 772 (Wyo. 1981))).

But the reality is very different. Fewer than half of states have a clearly stated approach.[108] Some states have explicitly rejected professional custom in favor of a general reasonableness inquiry for which custom is only probative information for a jury to consider, but over half of those states nevertheless appear to continue to defer to professional custom.[109] Meanwhile, some states adhering to professional custom have departed from it in practice by allowing a broader range of evidence than professional testimony to establish reasonableness.[110]

To gain a more complete picture of what an overall shift to a reasonableness standard would entail, we conducted a national survey of state law on customary practice. We conclude that professional custom continues to play a critical, and in many cases determinative, role in physician liability in up to three-quarters of the states.

1. Methodology

Our fifty-state survey of cases and statutes examines the role of customary practice in determining breach in medical malpractice.[111] Specifically, it examines (1) the current standard in every state; (2) if states have abandoned the customary practice standard, what they have replaced it with; (3) whether professional custom still is a driver of judicial outcomes in those states that have abandoned the professional custom standard; and (4) whether the scope of evidence is expanded to include more than customary practice in states with a professional custom standard. The data for this study was collected by running LexisNexis and Westlaw searches for cases and statutes current through June 11, 2024. The search terms were "prof! /3 custom."

108. *See infra* Part I.C.2.b.

109. *See infra* Part I.C.2.b.

110. *See infra* Part I.C.2.b.

111. State practice is not always clear. The survey examines relevant statutes and case law; when they appear to conflict, the state's approval is labeled as "unclear." Further, an articulated approach may not be what is employed by courts, and states in which that occurs are discussed in Part I.C.2.b. *See* Ani B. Satz & Liza Vertinsky, Fifty State Survey of Professional Custom in Medical Malpractice (2024) (unpublished survey) (on file with authors).

2. Results

The survey results are described below. Notably, about three-fourths of states adhere to the professional custom standard or have an unclear standard. Fifteen states have adopted the reasonableness test or a hybrid approach, with more than half of those states continuing to appeal to customary practice despite the stated change.

a. Summary

Our results indicate that twelve states adhere to professional custom doctrine, fourteen states have fully abandoned it, one state has a hybrid approach, and twenty-three states have unclear or conflicting law.[112] The states that have abandoned the professional custom standard have replaced it with either a reasonableness test (with varying language) or an explicit hybrid test (Louisiana).[113] In seven of the fourteen states that have fully abandoned the professional custom standard, professional custom continues to influence judicial outcomes.[114] Six of the twelve states with the professional custom standard have expanded the scope of evidence to include more than customary practice.[115]

112. *See infra* Table 1.

113. *See infra* Table 2.

114. These states are Colorado, Illinois, Indiana, Louisiana, Mississippi, Texas, Virginia, and Washington. *See infra* Table 2.

115. These states are Alaska, Massachusetts, Missouri, Montana, Nevada, and New York. *See infra* notes 142-48 and accompanying text.

Table 1. Breach of Standard of Care in Medical Malpractice Actions[116]

Breach Determined By:	Number of States	States
Professional Custom	Twelve (12)	Alaska, Arkansas, Idaho, Massachusetts, Missouri, Montana, Nevada, New Jersey, New Mexico, New York, North Dakota, South Dakota
Reasonableness Test	Fourteen (14)	Colorado, Florida, Illinois, Indiana, Maryland, Mississippi, Oregon, Rhode Island, Texas, Vermont, Virginia, Washington, Wisconsin, Wyoming
Hybrid Test	One (1)	Louisiana
Unclear	Twenty-three (23)	Alabama, Arizona, California, Connecticut, Delaware, Georgia, Hawaii, Iowa, Kansas, Kentucky, Maine, Michigan, Minnesota, Nebraska, New Hampshire, North Carolina, Ohio, Oklahoma, Pennsylvania, South Carolina, Tennessee, Utah, West Virginia

116. *See* Satz & Vertinsky, *supra* note 111.

Table 2. Reasonableness Test Language

State	Reasonableness Standard
Colorado*	"reasonably careful physician"[117]
Florida	"reasonably prudent physician"[118]
Illinois*	"ordinarily careful professional"[119]
Indiana*	"reasonably careful, skillful, and prudent practitioners"[120]
Louisiana*	Two tiers: (1) "degree of skill ordinarily employed, under similar circumstances, by the members of his profession," and (2) "reasonable care and diligence, along with his best judgment"[121]
Maryland	"reasonably competent practitioner"[122]
Mississippi*	"care ... [a] physician may reasonably be expected to possess"[123]
Oregon	"ordinarily careful physicians"[124]
Rhode Island	"reasonably competent practitioner"[125]
Texas*	"reasonable and prudent member of the medical profession[126]
Vermont	"reasonably skillful, careful, and prudent health care professional"[127]
Virginia*	"reasonably prudent practitioner"[128]
Washington*	"reasonably prudent health care provider"[129]
Wisconsin	"reasonable person"[130]
Wyoming	"skill, diligence and knowledge ... reasonably ... exercised and applied under similar circumstances by members of [the] profession"[131]

*States where professional custom still may drive judicial outcomes

117. Day v. Johnson, 255 P.3d 1064, 1069 (Colo. 2011).
118. Saunders v. Dickens, 151 So. 3d 434, 441 (Fla. 2014).
119. Advincula v. United Blood Servs., 678 N.E.2d 1009, 1020 (Ill. 1996).
120. Vergara v. Doan, 593 N.E.2d 185, 187 (Ind. 1992).
121. Meyer v. St. Paul-Mercury Indem. Co. of St. Paul, Minn., 73 So. 2d 781, 782 (La. 1953), *overruled on other grounds by* Ardoin v. Hartford Accident & Indem. Co., 360 So. 2d 1331 (La. 1978); *see also* Guy v. Bourgeois, 945 So. 2d 161, 164-65 (La. Ct. App. 2006).
122. Shilkret v. Annapolis Emergency Hosp. Ass'n, 349 A.2d 245, 253 (Md. 1975).
123. Hall v. Hilbun, 466 So. 2d 856, 872 (Miss. 1985).
124. OR. REV. STAT. § 677.095 (1) (2024).
125. Sheeley v. Mem'l Hosp., 710 A.2d 161, 167 (R.I. 1998).
126. Hood v. Phillips, 554 S.W.2d 160, 165 (Tex. 1977); *see also* Wheeler v. Aldama-Luebbert, 707 S.W.2d 213, 216-17 (Tex. App. 1986).
127. VT. STAT. ANN. tit. 12, § 1908 (1) (2024).
128. VA. CODE ANN. § 8.01-581.20 (A) (2024).
129. WASH. REV. CODE § 7.70.040(1)(a) (2021).
130. Nowatske v. Osterloh, 543 N.W.2d 265, 270 (Wis. 1996).
131. Vassos v. Roussalis, 625 P.2d 768, 772 (Wyo. 1981).

b. Breakdown

Judicial adherence to professional custom is varied and complicated. State courts differ with respect to whether they continue to follow professional custom. In addition, some states that have abandoned professional custom continue to appeal to it in practice. Meanwhile, other states that continue to adhere to professional custom have broadened the scope of evidence considered beyond physician practice.

Fourteen states have fully abandoned professional custom, and one state has adopted a hybrid approach. Courts in seven of the states that fully abandoned professional custom continue to appeal to professional custom to determine breach.[132] In Colorado, for example, "there is a presumption that adherence to the applicable [professional custom] constitutes due care for those practicing [the custom]."[133] The burden is on the party challenging the custom "to rebut the presumption by competent evidence."[134] A similar approach is taken in Illinois, Indiana, and Virginia. In Illinois, "[c]ustom is relevant in determining the standard of care because it illustrates what is feasible, it suggests a body of knowledge of which the defendant should be aware, and it warns of the possibility of far-reaching consequences if a higher standard is required."[135] According to another Illinois court, for cases involving "professional negligence, including hospital institutional negligence, custom and practice play a significant role."[136] In Indiana, to determine whether a doctor acted reasonably, courts consider locality and "advances in the profession," which are factors typically associated with professional custom.[137] Similarly, in Virginia, to determine whether a doctor acted reasonably, courts consider local practice.[138]

In Texas, Mississippi, and Washington, professional custom is given less weight but still considered part of a reasonableness test. In Texas, "evidence of the custom of medical care, while not

132. *See supra* Table 2.
133. United Blood Servs. v. Quintana, 827 P.2d 509, 521 (Colo. 1992) (en banc).
134. *Id.*
135. Darling v. Charleston Cmty. Mem'l Hosp., 211 N.E.2d 253, 257 (Ill. 1965).
136. Advincula v. United Blood Servs., 678 N.E.2d 1009, 1027 (Ill. 1996).
137. Vergara v. Doan, 593 N.E.2d 185, 187 (Ind. 1992).
138. Raines v. Lutz, 341 S.E.2d 194, 196 (Va. 1986).

conclusive, is some evidence of the standard of care."[139] In Mississippi and Washington, conformity with established medical custom is "evidence of performance of the duty of care," though not conclusive of such compliance.[140]

Louisiana has a unique approach, a two-tiered test that requires a physician to (1) exercise the skill "ordinarily employed" by similarly situated physicians "in good standing"; and (2) "use reasonable care and diligence" in the application of such skill.[141] This hybrid approach continues to embrace professional custom while also considering reasonableness in the exercise of professional custom.

Meanwhile, six states that have formally maintained the professional custom standard have strayed from it by expanding the scope of evidence to include more than customary practice. In Alaska,[142] Missouri,[143] Montana,[144] and Nevada,[145] courts have held physicians to the standard of care of a reasonable physician. For example, in Montana, physicians are held to the standard of a "reasonably competent general practitioner acting in the same or similar community in the United States in the same or similar circumstances."[146] And in Massachusetts and New York, a physician must "exercise [their own] judgment within the standard of care" (Massachusetts)[147] and reject custom when it does not align with a physician's "expertise or best judgment" (New York).[148]

139. Kissinger v. Turner, 727 S.W.2d 750, 755 (Tex. App. 1987).

140. Hall v. Hilbun, 466 So. 2d 856, 872 (Miss. 1985); *see* Harris v. Groth, 663 P.2d 113, 115 (Wash. 1983).

141. Meyer v. St. Paul-Mercury Indem. Co. of St. Paul, Minn., 73 So. 2d 781, 782 (La. 1953), *overruled on other grounds by* Ardoin v. Hartford Accident & Indem. Co., 360 So. 2d 1331 (La. 1978); LA. STAT. ANN. § 9:2794 (2003).

142. Titus v. Dep't of Corr., 496 P.3d 412, 419 (Alaska 2021).

143. Sillyman v. Barbe, 423 S.W.3d 304, 306 (Mo. Ct. App. 2014).

144. Chapel v. Allison, 785 P.2d 204, 210 (Mont. 1990).

145. Humboldt Gen. Hosp. v. Sixth Jud. Dist. Ct., 376 P.3d 167, 170 & n.2 (Nev. 2016).

146. *Chapel*, 785 P.2d at 210 (internal quotation marks omitted) (quoting Shilkret v. Annapolis Emergency Hosp. Ass'n, 349 A.2d 245, 253 (Md. 1975)).

147. Paiva v. Kaplan, 169 N.E.3d 1218, 1222 (Mass. App. Ct. 2021).

148. Toth v. Cmty. Hosp. at Glen Cove, 239 N.E.2d 368, 373 (N.Y. 1968).

II. INDUSTRY INFLUENCE OVER CUSTOM IN PRESCRIBING: CASE STUDIES

In this Part, we offer three case studies that provide examples of the ways in which pharmaceutical companies exert different pathways of influence over prescribing practices. This influence is designed to expand the scope and volume of drug prescriptions. In doing so, this affects, and in some cases alters, what is regarded as customary use of drugs.

The first case study, Thalomid, illustrates commercial influence over customary use of a drug by creating new off-label uses for a drug that had been taken off the market decades earlier due to safety concerns. It explores the consequences of aggressive off-label marketing to prescribers—combined with efforts to limit the entry of a generic competitor—on the evolution, costs, and risks of what becomes a customary cancer treatment.

The second case study, Zyprexa, also illustrates commercial influence over customary off-label use of a drug, but this time by creating a market for a drug within a vulnerable industry—nursing homes. Zyprexa is a psycho-pharmacological drug developed to treat psychosis that also has the effect of making patients easier to manage, requiring less human care. The synergies and converging interests of drug manufacturers, distributors, and nursing homes created an opportunity for both to profit from expanding the use of Zyprexa by nursing home residents.

The third case study, Aduhelm, illustrates efforts to shape what is considered customary use of a drug via influence over FDA approval of the drug and its label and influence over prescribing practices. It captures early industry efforts to influence the process of obtaining FDA approval to sell the drug and efforts to surmount regulatory hurdles to broaden its use.[149] While limits on reimbursement imposed by the Centers for Medicare and Medicaid Services (CMS) ultimately contributed to a limited market for this drug—and its maker Biogen subsequently withdrew it from the market—

149. *See, e.g.*, Daniel G. Aaron, *The Fall of FDA Review*, 22 YALE J. HEALTH POL'Y L. & ETHICS 95, 115-16, 121 (2023) (discussing concerns about weakening FDA independence due to industry pressure and faltering approval standards).

Biogen's efforts paved the way for expanded use of another, similar drug they introduced shortly thereafter, Leqembi.

In all three cases, the manufacturing company stands to gain significant revenue from expanding the range of uses for and users of its drug. This expansion plays a role in establishing customary use. While in some instances corporate influence over prescribing practices may simply augment effective uses of the drug and not cause patient harm, in other contexts, the distortion of prescribing decisions is detrimental to patients and wastes resources on ineffective care.

A. Thalomid: Commercially Engineered Off-Label Use to Establish Drug as Customary Cancer Treatment

> *Every woman in this country, I think, must be aware that it's most important that they check their medicine cabinet and that they do not take this drug.*
>
> —President John F. Kennedy, August 1, 1962[150]

This case study examines the commercially engineered push to turn thalidomide, a harmful drug pulled from the market, into a customary treatment for a variety of diseases. The early story of thalidomide illustrates the dangers of commercial interests in expanding markets for the drug without appropriate regulatory safeguards.[151] The later story shows the power of commercial interests to navigate, exploit, and sometimes circumvent these safeguards in pursuit of market growth.[152] The case study highlights the pathways of influence that Celgene exerted over prescribing to turn thalidomide into a widely used multi-billion dollar off-label cancer treatment.[153] It also shows how Celgene exploited the regulatory system to delay generic drug entry into the market, preserving its

150. British Pathé, *President Kennedy Calls for Stronger Drug Laws (1962)*, YOUTUBE (Apr. 13, 2014), https://www.youtube.com/watch?v=2fp5sGvCdVE [https://perma.cc/26DM-P5Y2].

151. *See infra* Part II.A.1.

152. *See infra* Part II.A.4.

153. Matthew Herper, *Celgene, Sold for $74 Billion, Leaves a Legacy of Chutzpah in Science and Drug Pricing*, STAT (Jan. 22, 2019), https://www.statnews.com/2019/01/22/celgene-legacy-chutzpah-science-drug-pricing/ [https://perma.cc/743X-C6N7].

brand name thalidomide drugs, Thalomid and Revlimid, as the customary treatments for some forms of cancer.[154]

1. First Commercial Push to Encourage Uses of Thalidomide in the U.S. Market

Thalidomide was developed by the Nazis during World War II.[155] It was later commercialized in West Germany and widely sold in Europe in the 1950s and 1960s as a sedative, as well as a treatment for asthma, hypertension, migraines, and morning sickness.[156] Despite the lack of safety testing, thalidomide was regarded as a safe and effective drug and "became almost as popular as aspirin" in some European countries.[157] In September 1960, U.S. company Richardson-Merrell applied for FDA approval to sell thalidomide as a sedative under the brand name Kevadon.[158]

Dr. Frances Oldham Kelsey, a newcomer to the FDA, was assigned to review the seemingly routine application.[159] While American drug approval was less rigorous at the time, and approvals were often routine, Dr. Kelsey became concerned by some of the safety data for the drug and requested more information from its U.S. manufacturers.[160] Richardson-Merrell resisted her requests, as the company had already provided one thousand physicians with

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154. Mark Terry, *Celgene's Once-Nightmare Drug Turned Blockbuster Returns*, BIOSPACE (Aug. 22, 2016), https://www.biospace.com/article/celgene-s-once-nightmare-drug-turned-blockbuster-returns/ [https://perma.cc/ZZE3-6NHQ]; *see* Herper, *supra* note 153.

155. Roger Williams, *The Nazis and Thalidomide: The Worst Drug Scandal of All Time*, NEWSWEEK (Sept. 10, 2012, 1:00 AM), https://www.newsweek.com/nazis-and-thalidomide-worst-drug-scandal-all-time-64655 [https://perma.cc/334Z-ELHY].

156. Chanapa Tantibanchachai, *US Regulatory Response to Thalidomide (1950-2000)*, EMBRYO PROJECT ENCYCLOPEDIA (Apr. 1, 2014), https://embryo.asu.edu/pages/us-regulatory-response-thalidomide-1950-2000 [https://perma.cc/QDX8-PWF2]; *see* Robert D. McFadden, *Frances Oldham Kelsey, Who Saved U.S. Babies from Thalidomide, Dies at 101*, N.Y. TIMES (Aug. 7, 2015), https://www.nytimes.com/2015/08/08/science/frances-oldham-kelsey-fda-doctor-who-exposed-danger-of-thalidomide-dies-at-101.html [https://perma.cc/9GN4-HGLE]; George J. Annas & Sherman Elias, *Thalidomide and the Titanic: Reconstructing the Technology Tragedies of the Twentieth Century*, 89 AM. J. PUB. HEALTH 98, 98-99 (1999).

157. Michael Winerip, *The Death and Afterlife of Thalidomide*, N.Y. TIMES (Sept. 23, 2013), https://www.nytimes.com/2013/09/23/booming/the-death-and-afterlife-of-thalidomide.html [https://perma.cc/7D27-RKAJ].

158. McFadden, *supra* note 156; Tantibanchachai, *supra* note 156.

159. *See* McFadden, *supra* note 156.

160. *See id.*

samples for "'investigational' research" and was storing Kevadon supplies in warehouses ready for marketing.[161]

By 1961, evidence of significant birth defects caused by thalidomide emerged in Europe.[162] Yet, Richardson-Merrell continued encouraging physicians to enroll their patients in clinical trials, even after learning that the German manufacturer, Chemie Grunenthal, was taking thalidomide off the market.[163] Indeed, Richardson-Merrell did not withdraw its application to sell the drug in the United States until March 1962, and continued to engage in efforts to bolster the reputation of Kevadon among physicians.[164] An FDA investigation into Richardson-Merrell's marketing activities revealed strong evidence that they had illegally promoted the drug prior to its approval.[165] According to an FDA investigator, "Richardson-Merrell employed many of the same tactics that modern-day drug companies have used to promote their products, the memos show, including hiring influential doctors to vouch for thalidomide, as well as helping the researchers to write scientific articles."[166]

While Richardson-Merrell was never prosecuted,[167] the thalidomide crisis spurred tighter drug regulation in the United States, resulting in a 1962 amendment to the Food, Drug, and Cosmetics Act.[168] The Kefauver-Harris Amendments of 1962 required more rigorous proof of safety and efficacy of new drugs and full disclosure

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161. *Id.*; *see* Tantibanchachai, *supra* note 156 ("[D]uring thalidomide's period of pending approval, Richardson-Merrell had already distributed greater than 2.5 million thalidomide tablets to over 1,200 physicians, who in turn gave them to approximately 20,000 patients in clinical trials."); *see also* Katie Thomas, *The Story of Thalidomide in the U.S., Told Through Documents*, N.Y. TIMES (Mar. 24, 2020), https://www.nytimes.com/2020/03/23/health/thalidomide-fda-documents.html [https://perma.cc/XC3J-9ECH].

162. *See* Tantibanchachai, *supra* note 156.

163. Thomas, *supra* note 161.

164. *Id.*

165. *Id.*

166. *Id.* (stating that the FDA reported the findings to the Department of Justice (DOJ) in July 1963 for criminal prosecution, including the claim that Richardson-Merrell had marketed an unapproved drug and claimed that it was safe, but the DOJ declined to prosecute the company).

167. *Id.*

168. Michelle Meadows, *Promoting Safe and Effective Drugs for 100 Years*, FDA CONSUMER MAG., (Jan.-Feb. 2006), https://www.fda.gov/about-fda/histories-product-regulation/promoting-safe-effective-drugs-100-years [https://perma.cc/37U8-2GQW].

of side effects.[169] At this time, thalidomide was banned worldwide ... at least for a while.[170]

2. Thalidomide Makes a Comeback: Betting the Business on Growing New Markets

Although thalidomide was not easily accessible after it was pulled from global markets, it remained in circulation and was informally tested as an experimental treatment for a variety of conditions, including some autoimmune disorders.[171] Despite its toxicity,[172] thalidomide's antiangiogenic (reducing blood vessel growth) and immunomodulatory (changing immune response) functions attracted continued research interest.[173] In 1964, a researcher provided anecdotal evidence that the drug might be effective in treating a skin disease associated with leprosy known as erythema nodosum leprosum (ENL).[174] In 1967, the World Health Organization ran a clinical trial on the use of thalidomide for leprosy,[175] where it found that the drug had some positive effects.[176] Subsequently, it was used to treat leprosy in several countries.[177] Thalidomide later became an FDA-approved treatment for ENL.[178] In the early 1990s, researchers

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169. *See id.*

170. Winerip, *supra* note 157.

171. *See* J. Blake Bartlett, Keith Dredge & Angus G. Dalgleish, *The Evolution of Thalidomide and its IMiD Derivatives as Anticancer Agents*, 4 NATURE REVS. CANCER 314, 314 (2004).

172. *See* Irene M. Ghobrial & S. Vincent Rajkumar, *Management of Thalidomide Toxicity*, 1 J. SUPPORTIVE ONCOLOGY 194 (2003) (providing a broad overview of thalidomide's toxic effects).

173. *See* Gerry Greenstone, *The Revival of Thalidomide: From Tragedy to Therapy*, 53 B.C. MED. J. 230 (2011).

174. *See id.*

175. C.G.S. Iyer, J. Languillon, K. Ramanujam, G. Tarabini-Castellani, J. Terencio de las Aguas, L.M. Bechelli, K. Uemura, V. Martinez Dominguez & T. Sundaresan, *WHO Coordinated Short-Term Double-Blind Trial with Thalidomide in the Treatment of Acute Lepra Reactions in Male Lepromatous Patients*, 45 BULL. WORLD HEALTH ORG. 719, 720 (1971).

176. *See id.* at 731-32.

177. *Thalidomide*, SCI. MUSEUM (Dec. 11, 2019), https://www.sciencemuseum.org.uk/objects-and-stories/medicine/thalidomide [https://perma.cc/6TYR-733Z].

178. Letter from Murray M. Lumpkin, Deputy Ctr. Dir., Ctr. for Drug Evaluation & Rsch., to Steve Thomas, Celgene Corp. (July 16, 1998), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/1998/20785ltr.pdf [https://perma.cc/5VN8-TWYQ]; Ronald L. Scott, *Thalidomide—Will Physicians Comply with FDA Rules?*, UNIV. HOUS. (July 23, 1998), https://www.law.uh.edu/healthlaw/perspectives/Food/980723Thalidomide.html [https://perma.cc/LUP6-

found that the antiangiogenic properties of thalidomide that had resulted in birth defects might make it useful in treating other disorders, including multiple sclerosis, Crohn's disease, and some cancers, such as multiple myeloma.[179]

Celgene, a subsidiary of a large chemical company, acquired the drug in the hope of finding new uses for it in the treatment of ENL and AIDS as well as broader, more profitable applications.[180] It was through Celgene's marketing efforts that thalidomide not only made it back onto the market, but also became a blockbuster treatment for certain cancers.

3. Celgene, the FDA, and Getting Thalidomide Back on the Market as Thalomid

Given its dangers, getting thalidomide back on the market as an approved drug was not an easy feat.[181] The entry point came in 1998, when the drug, with brand name Thalomid, received orphan drug approval for treatment of ENL.[182] In light of thalidomide's significant side effects, the drug's approval was accompanied by a costly FDA-required safe distribution system, or Risk Evaluation and Mitigation Strategies (REMS).[183] But this conditioned approval

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179. Winerip, *supra* note 157.

180. *See* Alison Kodjak, *How a Drugmaker Gamed the System to Keep Generic Competition Away*, NPR (May 17, 2018, 11:16 AM), https://www.npr.org/sections/health-shots/2018/05/17/571986468/how-a-drugmaker-gamed-the-system-to-keep-generic-competition-away [https://perma.cc/4CDR-LUJS]; Herper, *supra* note 153; *Celgene Corporation*, CO.-HISTS., https://www.company-histories.com/Celgene-Corporation-Company-History.html [https://perma.cc/T5SG-JY6T].

181. *See Celgene Corporation*, *supra* note 180; Jef Feeley & Doni Bloomfield, *From Nightmare Drug to Celgene Blockbuster, Thalidomide Is Back*, BLOOMBERG LAW (Aug. 22, 2016, 4:25 PM), https://news.bloomberglaw.com/health-law-and-business/from-nightmare-drug-to-celgene-blockbuster-thalidomide-is-back [https://perma.cc/BT88-WLX2] ("Recently unsealed documents in a lawsuit by a company saleswoman-turned-whistle-blower allege that its success is due to an aggressive campaign to encourage doctors to prescribe it and successor drugs to treat maladies beyond those the Food and Drug Administration authorized.").

182. *See* Stuart L. Nightingale, *Thalidomide Approved for Erythema Nodosum Leprosum*, 280 JAMA 872, 872 (1998); *Celegene Corporation*, *supra* note 180.

183. *See* Sheryl Gay Stolberg, *Thalidomide Approved to Treat Leprosy, with Other Uses Seen*, N.Y. TIMES (July 17, 1998), https://www.nytimes.com/1998/07/17/us/thalidomide-approved-to-treat-leprosy-with-other-uses-seen.html [https://perma.cc/2L39-52KM]; *Celgene Corporation*, *supra* note 180; Kodjak, *supra* note 180.

enabled Celgene to re-introduce thalidomide, marketed as Thalomid, to the U.S. market.[184]

Once on the market, Thalomid could be prescribed for off-label uses, and Celgene was free to sponsor research into uses of thalidomide in other areas.[185] Thalidomide's antiangiogenic properties suggested it could be important for treating cancer,[186] and cancer treatments were a lucrative section of the market, making them an attractive target for Celgene.[187] "As early as 1999, in its Annual Report to shareholders, Celgene announced that more than 90% of Thalomid prescriptions were for oncology, a purpose not approved by the FDA."[188]

4. Encouraging Off-Label Prescribing of Thalomid in Treating Cancer

Celgene was attracted to the cancer treatment market both because of its size and the comparatively high pricing opportunities for drugs.[189] Celgene's persistent efforts paid off in 2005—seven years after the approval of Thalomid for ENL—when Celgene obtained FDA approval for a new version of thalidomide, Revlimid.[190] Then,

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184. *Celgene Corporation*, *supra* note 180.

185. *See* Stolberg, *supra* note 183.

186. Bartlett et al., *supra* note 171, at 315 (stating that a breakthrough for thalidomide in oncology came in 1994 when researchers from pioneering scientist Judah Folkman's lab discovered that thalidomide could inhibit angiogenesis, which earlier research indicated was important for treating cancer, and that the drug ultimately ended up in a clinical trial for patients with multiple myeloma).

187. *See* STAFF OF H. COMM. ON OVERSIGHT AND REFORM, 116TH CONG., DRUG PRICING INVESTIGATION: CELGENE AND BRISTOL MYERS SQUIBB-REVLIMID 29 (Comm. Print 2020) ("An internal 'Strategic Rationale' memorandum from April 2009 ... emphasized the 'Financial Opportunity' of the investment [in targeting newly diagnosed multiple myeloma patients].... The memorandum concluded: 'No other current or planned Celgene program approaches the financial value represented by realizing the assumptions in our current newly diagnosed multiple myeloma global sales forecast.'").

188. Third Amended Complaint at 3, United States *ex rel.* Brown v. Celgene Corp., 226 F. Supp. 3d 1032 (C.D. 2016) (No. 2:10-cv-03165); *see also id.* at 2 (referencing FDA warning letters Celgene received in 1998 and 2000).

189. *See, e.g.*, Eric Sagonowsky, *Celgene Repeatedly Raised Revlimid's Price to Hit Aggressive Sales Targets, Congressional Probe Finds*, FIERCE PHARMA (Sept. 30, 2020, 9:30 AM), https://www.fiercepharma.com/pharma/celgene-repeatedly-raised-revlimid-s-price-to-meet-aggressive-sales-targets-congressional [https://perma.cc/EHK4-3SWS].

190. *See* Judith Stewart, *Revlimid FDA Approval History*, DRUGS.COM (Sept. 7, 2020), https://www.drugs.com/history/revlimid.html [https://perma.cc/V9KW-Y58H].

in 2006, Thalomid was approved as part of a drug combination to treat multiple myeloma.[191]

But Celgene had not been waiting for FDA approval to promote thalidomide as a cancer drug. Long before Celgene received FDA approval, even for these limited forms of cancer, it was pursuing a marketing campaign in which the company encouraged off-label prescribing of Thalomid for a variety of cancers.[192] From the time it received its first marketing approval for ENL, off-label prescriptions for the drug as a cancer treatment were the driver of Thalomid sales. According to an SEC filing, "In 2000, six years before Thalomid was approved as a cancer treatment, oncological cases accounted for 92 percent of prescriptions."[193] "In 2004, then-CFO Robert Hugin told investors the drug was the company's 'financial engine.'"[194] Celgene's marketing activities and pricing strategies were driven by aggressive sales targets and earnings incentives, a strategy that was yielding almost $8 billion in sales by 2018.[195]

More specifically, once the FDA approved Thalomid's sale as an ENL treatment, Celgene allegedly pursued strategies that included off-label marketing of Thalomid for cancer treatment and the payment of kickbacks to physicians prescribing the drug to cancer patients.[196] Furthermore, Celgene purportedly failed to warn physicians adequately about safety concerns surrounding the drug's use.[197] While Celgene was aware of serious risks that the drug posed to cancer patients, there is evidence that Celgene did not highlight

191. *FDA Approval for Thalidomide*, NAT'L CANCER INST. (July 3, 2013), https://web.archive.org/web/20150705222948/https://www.cancer.gov/about-cancer/treatment/drugs/fda-thalidomide [https://perma.cc/AK5N-8SLE]; Herper, *supra* note 153.

192. *Brown*, 226 F. Supp. 3d at 1037-38 ("Thalomid was not approved to treat any form of cancer until May 2006 .... Nonetheless, Celgene began to promote Thalomid for off-label cancer uses almost immediately after obtaining FDA approval for use in ENL cases [in 1998]."). For a description of some of the practices that Celgene was alleged to have engaged in, see *id.* at 1037-40, the summary of facts in the whistleblower case brought against it by former employee Brown.

193. Feeley & Bloomfield, *supra* note 181.

194. *Id.*

195. *See* Sagonowsky, *supra* note 189 ("But if the company's goal was to grow its multiple myeloma business to $8 billion, the strategy worked. In 2018—two years ahead of the 2020 target—the franchise hit $7.8 billion on a massive $6.46 billion contribution from Revlimid.").

196. *Brown*, 226 F. Supp. 3d at 1036.

197. *See* Third Amended Complaint, *supra* note 188, at 32-36; *see also* Y. Tony Yang, Brian Chen & Charles L. Bennett, *Thalidomide, Drug Safety, and Off-Label Prescribing: Lessons Learned from Celgene's Settlement*, 4 JAMA ONCOLOGY 915, 915 (2018).

these risks when encouraging physicians to use the drug in oncology.[198]

Meanwhile, Celgene grew its sales force from twenty people in 1998, to one hundred by 2002.[199] The sales force was trained in uses of thalidomide for cancer treatment and engaged in a variety of marketing tactics designed to encourage off-label prescriptions, including discussing literature exploring uses of thalidomide to treat cancer.[200] "Celgene evaluated sales representatives based on their success in convincing physicians to prescribe Thalomid and Revlimid and compensated representatives based on their sales volume."[201]

Celgene focused its marketing efforts on encouraging physician use of Thalomid not only for multiple myeloma, but for other blood cancers, and even cancers more generally. In both 1999 and 2000, Celgene produced marketing plans that included "preparing 'sales materials' for oncologists and hematologists" engaged in cancer treatment, sharing these materials at conferences, and publishing in journals that catered to these specialists.[202] The 2000 plan stated that Celgene should "legitimize Thalomid as a treatment option for a variety of tumor types ... while supporting the focused activity of our field force in [multiple myeloma]."[203] Subsequently, "The 2004 Business Plan for the West Region set specific sales goals for off-label uses of Thalomid, and urged representatives to discuss off-label cancer uses 'on every call.'"[204] Celgene's marketing efforts allegedly included providing financial support to generate literature showing anecdotal support for off-label use of Thalomid in treating various cancers that could be shared with prescribers during sales visits.[205]

On April 27, 2010, a *qui tam* action was brought "on behalf of the United States, twenty-four states, the District of Columbia, and the

198. *See* Third Amended Complaint, *supra* note 188, at 32-36; *see also* Yang et al., *supra* note 197.

199. *Brown*, 226 F. Supp. 3d at 1038.

200. *See id.* at 1038-39.

201. *Id.* at 1039 (footnote omitted).

202. *Id.* at 1038.

203. *Id.* (omission in original).

204. *Id.*

205. *See id.* at 1036; Third Amended Complaint, *supra* note 188, at 49-50.

City of Chicago" against Celgene, based on its alleged off-label sales.[206] Court proceedings established that "Celgene's sales representatives made between 4,000 and 5,000 physician contacts per month, with nearly 80% of these contacts involving hematology-oncology or oncology specialists."[207] This strategy was successful, as "Celgene sold between 800,000 and 1,000,000 Thalomid capsules per month, almost exclusively for off-label uses (99.75% of sales between 2001 and 2005 were for off-label uses)."[208] Celgene is also alleged to have "paid kickbacks—in the form of speaker fees, paid clinical trials, advisory board positions, and authorship of ghost-written articles—to physicians in exchange for prescriptions of its drugs."[209] Most importantly, "physicians who received more promotional contacts prescribed at a higher rate than those who received fewer contacts,"[210] indicating the ability of Celgene to influence professional custom and, ultimately, the legal standard of care.

The FDA sent warning letters to Celgene in 1998, and again in 2000, expressing concerns about Celgene's off-label marketing of Thalomid as well as its failure to state the risks of the drug adequately.[211] Nevertheless, Celgene persisted with its marketing strategies. When marketing Thalomid and later Revlimid, Celgene is alleged to have knowingly concealed the risks of venous thromboembolism and death caused by these drugs in cancer treatment.[212]

Despite the lack of evidence of efficacy and concerns about safety, Celgene successfully encouraged physician use of Thalomid and Revlimid for off-label use in the treatment of blood cancer to such an extent that, for some types of blood cancer, these drugs became customary use, even before receiving approval for a limited subset of cancers. Between 1998, when thalidomide was first approved to

206. *Brown*, 226 F. Supp. 3d at 1035-36.

207. *Id.* at 1039.

208. *Id.* (citation omitted).

209. *Id.* at 1036.

210. *Id.* at 1040.

211. *See* Third Amended Complaint, *supra* note 188 ("The FDA was particularly concerned about Celgene's conduct relating to Thalomid because '[p]erhaps more than for any other available drug, the need to provide and distribute thalidomide responsibly is essential to the public health.'" (alteration in original) (quoting Letter from Thomas W. Abrams, Dir., Div. of Drug Mktg., Advert. & Commc'ns, FDA, to John W. Jackson, CEO, Celgene Corp. (Apr. 21, 2000))).

212. *See id.* at 4, 28.

treat ENL, and 2006, when Celgene received an FDA indication for Thalomid to treat multiple myeloma, the drug was generating millions of dollars in revenue.[213] Soon thereafter, Thalomid was replaced by Revlimid, which Celgene sold at a higher price.[214]

In 2017, the judicial proceedings against Celgene ended in a $280 million settlement[215]—the second largest financial settlement of a pharmaceutical safety and off-label marketing case at the time.[216] The effect of this settlement on corporate practice remains unclear.

5. Ensuring Continued Prescriptions of Thalomid and Revlimid by Keeping Generics Off the Market

Once Celgene received FDA approval for Thalomid and Revlimid to treat limited cancers, it had an interest in limiting the entry of generic versions that would compete with its brand-named drugs. Celgene used aggressive tactics to deter or delay the entry of alternative treatments, thus preserving its monopoly over thalidomide and exploiting its use as a customary treatment that lacked alternatives.[217]

Celgene used its prolonged monopoly position to increase the price of thalidomide over time.[218] When the FDA first approved thalidomide for ENL treatment, it was $6 per pill.[219] As the effectiveness of thalidomide in oncology became established, Celgene continued to raise the price of Thalomid and then Revlimid.[220] As a result, "Celgene has been able to continue reaping as much as $170 to $310 per dose for Thalomid and $430 per dose for Revlimid, or

213. *See* Herper, *supra* note 153.

214. *See id.*

215. Press Release, U.S. Att'y's Off., C.D. Cal., Celgene Agrees to Pay $280 Million to Resolve Fraud Allegations Related to Promotion of Cancer Drugs for Uses Not Approved by FDA (July 24, 2017), https://www.justice.gov/usao-cdca/pr/celgene-agrees-pay-280-million-resolve-fraud-allegations-related-promotion-cancer-drugs [https://perma.cc/H6HR-LD68].

216. Yang et al., *supra* note 197.

217. *See* Kodjak, *supra* note 180.

218. *See* STAFF OF H. COMM. ON OVERSIGHT AND REFORM, *supra* note 187, at i ("Since launching Revlimid in 2005, Celgene raised the price of the drug 22 times, from $215 per pill to $719 per pill.... Due to Revlimid price increases, from 2009 to 2018, Celgene reported over $51 billion in net worldwide revenue from Revlimid, with the U.S. market accounting for $32 billion of that total.").

219. Herper, *supra* note 153.

220. *Id.*

more than $200 million annually for Thalomid and $4 billion annually for Revlimid."[221] By 2017, Revlimid generated $8.1 billion in profits for Celgene,[222] and by 2019, it was $693 per pill.[223]

Despite the rebranded versions of thalidomide being available for over a decade by 2017—and thalidomide itself for decades before that—Celgene was successfully able to sustain this price by avoiding generic competition and maintaining a monopoly.[224] The usual patent term is twenty years, so Celgene could not maintain a monopoly with a patent alone.[225] Instead, Celgene pursued market exclusivity strategies, combined with patents on new versions of thalidomide, and on its method of distribution, or REMS.[226] Celgene also found ways to ensure separate, overlapping orphan drug approvals for the treatment of rare diseases by thalidomide to extend its market exclusivity another seven years with each approval.[227] Additionally, Celgene limited the ability of generic competitors to obtain necessary samples of the drug for the requisite comparisons to bring a generic onto the market,[228] and when Celgene was unable to block access, it made deals with the potential competitors to stay off the market.[229] By restricting competition, Celgene was able to continue increasing its drug prices over time: "With persistent price increases, quarter after quarter, Celgene pioneered ... 'modern pricing.' Cancer drug prices have risen inexorably."[230]

Celgene built and sustained a multi-billion-dollar market for a dangerous drug through its aggressive marketing strategies. From

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221. Kodjak, *supra* note 180.

222. *Id.*

223. Herper, *supra* note 153.

224. *See* Kodjak, *supra* note 180.

225. *See Frequently Asked Questions on Patents and Exclusivity*, FDA (Feb. 5, 2020), https://www.fda.gov/drugs/development-approval-process-drugs/frequently-asked-questions-patents-and-exclusivity [https://perma.cc/6KZC-DEYR].

226. *See* Kodjak, *supra* note 180.

227. *See id.*; 21 C.F.R. § 316.31(a) (2023) (establishing a seven-year orphan drug exclusive approval period).

228. *How Celgene Uses Safety Concerns to Keep Its $7 Billion Cancer Drug on Top*, MLEX (Jan. 12, 2018), https://mlexmarketinsight.com/news-hub/editors-picks/area-of-expertise/antitrust/how-celgene-uses-safety-concerns-to-keep-its-$7-billion-cancer-drug-on-top [https://perma.cc/JJ3H-4BGY].

229. Kodjak, *supra* note 180.

230. Herper, *supra* note 153.

the start, Celgene's focus was on maximizing the commercial potential of thalidomide by establishing it as a treatment in profitable disease areas, such as cancer. Celgene focused on selling Thalomid, and the related drug Revlimid, in niche cancer markets where there were, at the time, few alternatives for patients. Celgene influenced the prescribing practices of the drug in oncology prior to approval of the drug for limited types of cancer and continued to push thalidomide for broader types of cancer after approval. While thalidomide did have properties that made it an effective treatment for certain diseases, Celgene's fervent focus on profit led to marketing and prescribing of the drug without an adequate balance of the risks and benefits for different diseases and patient groups or attention to and management of the risks associated with its use. Marketing thalidomide off-label was especially dangerous, given its known risks. Celgene also used aggressive tactics to deter or delay the entry of both alternative and generic treatments that might compete with thalidomide, further preserving the role of Thalomid and Revlimid as a customary treatment.

B. Zyprexa: Commercially Driven Expansion of Antipsychotic Treatments in Nursing Homes and the Failure to Reset Customary Use

> *Every medical treatment has a glimpse of mystery in it, the ghost lingering in the algorithm, but psychiatry is even closer to alchemy than most.*[231]

In 2021, a *New York Times* investigation exposed the overuse of antipsychotics in nursing homes, with at least 21 percent of nursing home residents being administered these drugs, many to their detriment.[232] According to 2020 numbers, more than one in five nursing home residents in many states, and one in ten residents at lowest in other states, had received antipsychotic medication within the

231. Ben Wallace-Wells, *Bitter Pill: How the Pharmaceutical Industry Turned a Flawed and Dangerous Drug into a $16 Billion Bonanza*, ROLLING STONE, Feb. 5, 2009, at 56.

232. Katie Thomas, Robert Gebeloff & Jessica Silver-Greenberg, *Phony Diagnoses Hide High Rates of Drugging at Nursing Homes*, N.Y. TIMES (Mar. 12, 2024), https://www.nytimes.com/2021/09/11/health/nursing-homes-schizophrenia-antipsychotics.html [https://perma.cc/ KR47-2W73].

last seven days.[233] This number did not reflect nursing home residents who were receiving antipsychotic drugs to treat schizophrenia, the primary approved use, nor did it include those being treated for Huntington's Disease and Tourette's Syndrome.[234] It also did not reflect those nursing home residents who received a misdiagnosis of schizophrenia, sometimes used as a way of avoiding reporting requirements for antipsychotic drugs.[235] Further, studies suggest that using these drugs to treat older patients with dementia carries increased risks of mortality, and the FDA has required a black box warning (its highest) against uses in this patient population for decades.[236] Despite these risks, nursing homes use antipsychotic drugs to treat behavioral symptoms, such as agitation associated with dementia, or to sedate their residents as a way of managing under-staffing.[237]

Zyprexa is one among a handful of newer antipsychotic drugs[238] that have become widely used in nursing homes.[239] Other well-known drugs in this category include Seroquel and Risperdal.[240] The manufacturers of these drugs played a significant role in driving the expansion of their use through a myriad of pathways of influence.

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233. *See MDS Frequency Report: Fourth Quarter 2020*, CTRS. FOR MEDICARE & MEDICAID SERVS., https://web.archive.org/web/20230602121309/https://www.cms.gov/apps/mds/mds_notemp/mds30FreqStart.asp?isSubmitted=mds30Freq3&var=N0410A&date=37 [https://perma.cc/XX9R-FFWR].

234. OFF. OF THE INSPECTOR GEN., U.S. DEP'T OF HEALTH & HUM. SERVS., OEI-07-19-00490, CMS COULD IMPROVE THE DATA IT USES TO MONITOR ANTIPSYCHOTIC DRUGS IN NURSING HOMES 3 (2021), https://oig.hhs.gov/oei/reports/OEI-07-19-00490.pdf [https://perma.cc/8Y27-TWEN].

235. *Id.* at 5, 8-9; Thomas et al., *supra* note 232.

236. *See, e.g.*, Martin Steinberg & Constantine G. Lyketsos, *Atypical Antipsychotic Use in Patients with Dementia: Managing Safety Concerns*, 169 AM. J. PSYCHIATRY 900, 900 (2012).

237. *See* T. Joseph Mattingly II, *A Review Exploring the Relationship Between Nursing Home Staffing and Antipsychotic Medication Use*, 4 NEUROLOGY & THERAPY 169, 170-71, 173 (2015); Elaine K. Howley, *Antipsychotic Drugs in Nursing Homes*, U.S. NEWS (Nov. 13, 2023), https://health.usnews.com/health-news/best-nursing-homes/articles/antipsychotic-use-in-nursing-homes [https://perma.cc/RE7P-3GHU]; HUM. RTS. WATCH, "THEY WANT DOCILE": HOW NURSING HOMES IN THE UNITED STATES OVERMEDICATE PEOPLE WITH DEMENTIA 25-26, 70 (2018), https://www.hrw.org/report/2018/02/05/they-want-docile/how-nursing-homes-united-states-overmedicate-people-dementia [https://perma.cc/WUN5-MGAV].

238. *See Atypical Antipsychotic Drugs Information*, FDA (May 10, 2016), https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/atypical-antipsychotic-drugs-information [https://perma.cc/Q5KV-KW4A].

239. HUM. RTS. WATCH, *supra* note 237, at 114.

240. *Atypical Antipsychotic Drugs Information*, *supra* note 238.

The magnitude of the corporate role in both directly and indirectly driving the prescription of these antipsychotics beyond their roots in the treatment of schizophrenia was exposed by recent cases involving overuse among the most vulnerable communities[241]: children in foster care[242] and older people in nursing homes.[243]

This case study focuses on the story of how new markets were created for Zyprexa by growing its off-label use in nursing homes as an anti-anxiety medication and sedative. It chronicles criminal cases and regulatory interventions exposing and attempting to prevent these uses. Despite these interventions[244] and the settlement of lawsuits against drug manufacturers who promoted Zyprexa's use in nursing homes for patients without schizophrenia,[245] Zyprexa continues to be prescribed in nursing homes for anxiety and sedation, although at a reduced level.[246]

1. Eli Lilly's Role in Shaping, Funding, and Framing the Research Supporting the Rise of Zyprexa

The story of how Zyprexa and other atypicals became a multibillion-dollar market suggests that the medical community—doctors, researchers, the institutions that back them—may be themselves prone to a placebo effect: the willed conviction that

241. *See, e.g.*, Thomas et al., *supra* note 232.

242. *See, e.g.*, Wallace-Wells, *supra* note 231.

243. *See, e.g.*, Press Release, U.S. Dep't of Just., Eli Lilly and Company Agrees to Pay $1.415 Billion to Resolve Allegations of Off-Label Promotion of Zyprexa (Jan. 15, 2009), https://www.justice.gov/archive/opa/pr/2009/January/09-civ-038.html [https://perma.cc/7YAC-5TJU].

244. Howley, *supra* note 237; *National Partnership to Improve Dementia Care in Nursing Homes*, CTRS. FOR MEDICARE & MEDICAID SERVS., https://www.cms.gov/medicare/health-safety-standards/quality-safety-oversight-general-information/national-partnership-improve-dementia-care-nursing-homes [https://perma.cc/DHA4-RBKE].

245. Press Release, U.S. Dep't of Just., Nation's Largest Nursing Home Pharmacy and Drug Manufacturer to Pay $112 Million to Settle False Claims Act Cases (Nov. 3, 2009), https://www.justice.gov/opa/pr/nation-s-largest-nursing-home-pharmacy-and-drug-manufacturer-pay-112-million-settle-false [https://perma.cc/R7EM-6FYC]; Press Release, U.S. Dep't of Just., *supra* note 243.

246. *See National Partnership to Improve Dementia Care in Nursing Homes: Antipsychotic Medication Use Data Report (April 2022)*, CTRS. FOR MEDICARE & MEDICAID SERVS., https://www.cms.gov/files/document/antipsychotic-medication-use-data-report-2021q4-updated-07292022.pdf [https://perma.cc/3B3Y-DREC].

> *a new drug, presented as a breakthrough, must in fact be one, that a product sold as healing must in fact do good.*[247]

Olanzapine, later known by brand name Zyprexa, was among the newly emerging atypical antipsychotic drug candidates being developed in the 1990s. It showed the same potential of existing treatments like clozapine for treating schizophrenia, but without the neurological toxicity associated with older antipsychotic treatments.[248] Eli Lilly was developing olanzapine in its labs just as the patents covering its blockbuster drug, Prozac, were set to expire.[249] Prozac accounted for about one-third of the company's profits prior to its patent expiration in 2001, and Eli Lilly was seeking a new blockbuster drug to replace the billions in revenue it would lose once generic manufacturers entered the market with cheaper substitutes for Prozac.[250]

From the start of its work on olanzapine, Eli Lilly sought to generate demand in the medical community for the new atypical antipsychotic drug. It selected and funded psychiatrists at a variety of universities to conduct clinical trials on olanzapine for schizophrenia treatment.[251] While the stated intention was to seek external validation for olanzapine, the likelihood of finding drug efficacy in such trials is high; studies have found that clinical trials funded by the company seeking approval are four times more likely to find drug efficacy than those that are independently funded.[252] Moreover, psychiatrists in need of more effective treatments for complex, poorly understood diseases, such as schizophrenia, are more prone to believe in the potential of the new atypical antipsychotics[253]: "[W]hen the system fails, the cause is often not outright deceit, but

247. Wallace-Wells, *supra* note 231.

248. Leslie Citrome, Joseph P. McEvoy, Mark S. Todtenkopf, David McDonnell & Peter J. Weiden, *A Commentary on the Efficacy of Olanzapine for the Treatment of Schizophrenia: The Past, Present, and Future*, 15 NEUROPSYCHIATRIC DISEASE & TREATMENT 2559, 2559-60 (2019).

249. Wallace-Wells, *supra* note 231.

250. *Id.*

251. *Id.*

252. *Id.*; *see also* Johnson, *supra* note 95, at 87, 89.

253. Tim Kendall, *The Rise and Fall of the Atypical Antipsychotics*, 199 BRIT. J. PSYCHIATRY 266, 267 (2011) ("The concept of atypicality, associated with the revival of clozapine, gave hope that there would be a class of drugs with less severe side-effects, especially EPS and tardive dyskinesia. Atypicality also provided a powerful marketing tool for the industry.").

rather a web of overbright enthusiasm, the urge that researchers have to convince themselves that a drug is a little better than it actually is, that it can save lives."[254]

2. Industry Role in Downplaying Adverse Effects

During the early studies of Zyprexa, evidence emerged that the drug caused significant weight gain, creating a risk of elevated blood sugar levels (hyperglycemia) for patients.[255] Eli Lilly took measures to downplay these effects, both in its 1995 application to the FDA for new drug approval, and its communications with doctors and the public.[256] Subsequently, the FDA approved Zyprexa for the treatment of schizophrenia and bipolar disorder in 1996.[257]

As a result of Eli Lilly's efforts to obscure Zyprexa's risks, the FDA's approved label did little to warn doctors and consumers about weight gain and hyperglycemia.[258] While the FDA later sent warning letters to Eli Lilly about the misleading nature of the company's claims that Zyprexa was safer than other antipsychotics and had limited side effects, Eli Lilly did not respond until a government report forced the issue.[259] In 2005, the FDA issued a general advisory about weight gain and hyperglycemia as well as a black box warning concerning the risks that atypical antipsychotics pose to older people with dementia.[260] Two years later, the FDA pushed Eli Lilly to revise the Zyprexa label to issue new warnings about the risks of weight gain and hyperglycemia associated with the drug.[261]

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254. Wallace-Wells, *supra* note 231.

255. *See id.*

256. *See* Mary Williams Walsh, *Judge to Unseal Documents on the Eli Lilly Drug Zyprexa*, N.Y. TIMES (Sept. 5, 2008), https://www.nytimes.com/2008/09/06/business/06lilly.html [https://perma.cc/J7J3-6PVD].

257. *See* Wallace-Wells, *supra* note 231.

258. *Id.*

259. *See id.*

260. *See* Peggy Peck, *FDA Warns of Excess Mortality to Elderly with Antipsychotics*, MEDPAGE TODAY (Apr. 12, 2005), https://www.medpagetoday.com/neurology/alzheimersdisease/870 [https://perma.cc/AXB5-EZS4].

261. *See* Press Release, Eli Lilly & Co., Lilly Announces Updates to the Zyprexa and Symbyax U.S. Labels (Oct. 5, 2007), https://investor.lilly.com/news-releases/news-release-details/lilly-announces-updates-zyprexa-and-symbyax-us-labels [https://perma.cc/KX4P-RZ8E].

The full extent of Eli Lilly's role in downplaying, obscuring, or even hiding the negative effects of Zyprexa became apparent only through lawsuits brought by thousands of people who claimed that they had developed diseases, including diabetes, as a result of being treated with Zyprexa.[262] They argued that Eli Lilly failed to disclose the risks associated with Zyprexa and engaged in off-label marketing of the drug for uses outside its approved indications.[263] Documents obtained in litigation revealed ways in which Eli Lilly minimized or hid the risks associated with Zyprexa while encouraging prescriptions for over a decade, stretching from when Eli Lilly received its first, albeit limited, approval for sale of the drug in 1996.[264]

In 1999, for example, Eli Lilly's chief scientist in charge of the company's program for Zyprexa acknowledged in internal email correspondence that the weight gain and potential for high blood sugar posed a threat to the long-term commercial success of the drug.[265] Internal disclosure of documents, "which include e-mail, marketing material, sales projections and scientific reports—are replete with references to Zyprexa's importance to Lilly's future and the need to keep concerns about diabetes and obesity from hurting sales."[266] Investigative journalism reveals that between 1995 and 2004, "Lilly's own published data, which it told its sales representatives to play down in conversations with doctors, [shows] that 30 percent of patients taking Zyprexa gain 22 pounds or more after a year on the drug, and some patients have reported gaining 100 pounds or more."[267] The same documents indicate that "Lilly was concerned that Zyprexa's sales would be hurt if the company was more forthright about the fact that the drug might cause unmanageable weight gain or diabetes."[268] Similarly, internal documents revealed that, while Eli Lilly researchers acknowledged the higher

262. *See* Alex Berenson, *Lilly Settles with 18,000 Over Zyprexa*, N.Y. TIMES (Jan. 5, 2007), https://www.nytimes.com/2007/01/05/business/05drug.html [https://perma.cc/5LGH-MMG7].

263. *See id.*

264. *Id.*

265. Alex Berenson, *Eli Lilly Said to Play Down Risk of Top Pill*, N.Y. TIMES (Dec. 17, 2006), https://www.nytimes.com/2006/12/17/business/17drug.html [https://perma.cc/4S96-G6KT].

266. *Id.*

267. *Id.*

268. *Id.*

risk of death Zyprexa posed to older dementia patients and the drug's lack of efficacy for treating dementia, its marketing strategy continued targeting older patients, because they were a significant source of revenue.[269]

3. Off-Label Marketing to Physicians

Even before it obtained FDA approval to market Zyprexa for schizophrenia, Eli Lilly was laying the foundation for a one billion dollar annual market in off-label sales.[270] In 2000, Eli Lilly began a multi-year promotional campaign called "Viva Zyprexa" targeting primary care physicians, even though there were almost no approved uses for Zyprexa in the primary health care market.[271] Around 59,000 primary care doctors were selected as targets for this program.[272] A marketing message was designed for them that emphasized the broad range of symptoms that might lend them to prescribe the drug: "Zyprexa: The safe, proven solution in mood, thought, and behavior disorders."[273] Eli Lilly's sales representatives were encouraged to promote Zyprexa by focusing on the treatment of symptoms such as agitation, rather than discussing Zyprexa's approved indications.[274] Broadening Zyprexa's possible indications further, "A key strategy in this campaign was the use of hypothetical patient profiles in detailing visits, most of which clearly failed to meet diagnostic criteria for any recognized mental disorder."[275] Litigation documents allege that Eli Lilly also spent millions of

269. Derek Lowe, *Selling Zyprexa*, SCI. (June 12, 2009, 7:58 AM), https://www.science.org/content/blog-post/selling-zyprexa [https://perma.cc/5WKG-XKB2].

270. Wallace-Wells, *supra* note 231 ("During the late 1990s, and then with increasing speed during the current decade, Wirshing and other psychiatrists watched as the market for atypical antipsychotics swelled well beyond its marked territory, far exceeding the country's supply of schizophrenic brains—past $2 billion a year, $5 billion, $10 billion, all the way to $16 billion. What had begun as niche drugs are now the third-largest class of medication in the world, their sales greater than those of the antidepressants.").

271. *See* Alex Berenson, *Drug Files Show Maker Promoted Unapproved Use*, N.Y. TIMES (Dec. 18, 2006), https://www.nytimes.com/2006/12/18/business/18drug.html [https://perma.cc/3MUG-M4DR].

272. Glen I. Spielmans, *The Promotion of Olanzapine in Primary Care: An Examination of Internal Industry Documents*, 69 SOC. SCI. & MED. 14, 15 (2009).

273. *Id.*

274. *Id.* at 14, 16.

275. *Id.* at 14.

dollars funding continuing medical education programs designed to promote off-label uses of Zyprexa.[276] Additionally, Zyprexa was marketed off-label as a treatment for dementia, despite its life-threatening risks.[277]

4. Synergies Between Commercial Needs of Drug Manufacturer and Nursing Homes

As early as 1999, Eli Lilly invested in the development of its long-term care sales force, which focused on promoting Zyprexa in nursing homes and assisted living facilities.[278] The company focused its sales efforts on encouraging doctors to prescribe Zyprexa to treat a range of disorders including "dementia, Alzheimer's dementia, depression, anxiety, and [insomnia]," as well as to address troubling "behavioral symptoms such as agitation, aggression, and hostility."[279] As a result, demand for Zyprexa in nursing home settings was often driven by the desire to treat behavioral symptoms, such as agitation associated with dementia, rather than psychosis.[280]

During its marketing campaign, Viva Zyprexa, sales representatives were told to suggest Zyprexa for older dementia patients, as nursing homes provided an opportunity for significant market expansion.[281] At the same time, nursing homes "are in a position to advocate for initiation and discontinuation of antipsychotics,"[282] and they have economic reasons to expand the use of these drugs as a

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276. Press Release, U.S. Dep't of Just., *supra* note 243.

277. Berenson, *supra* note 271.

278. Press Release, U.S. Dep't of Just., *supra* note 243.

279. *Id.*

280. *See* Peck, *supra* note 260 ("These drugs are typically used off-label in nursing homes to control 'sundowning.' In this condition patients with dementia wander the halls and develop agitation during nighttime hours.").

281. Berenson, *supra* note 271; *see The Primary Care Opportunity*, UCSF INDUS. DOCUMENTS LIBR.: DRUG INDUS. DOCUMENTS, https://industrydocuments.ucsf.edu/drug/docs/#id=fnbn0217 [https://perma.cc/Q85Y-M9HE]; *see also* Jim Edwards, *Eli Lilly Promoted Zyprexa for Patients Who Were Badly Dressed*, CBS NEWS (June 4, 2009, 4:44 PM), https://www.cbsnews.com/news/eli-lilly-promoted-zyprexa-for-patients-who-were-badly-dressed/ [https://perma.cc/5VS7-LUBR].

282. Yan Zhang, Elena M. Letuchy & Ryan M. Carnahan, *Where Are Antipsychotics Prescribed in Nursing Homes Initiated?*, 66 J. AM. GERIATRICS SOC'Y 1082, 1082 (2018) (examining where the initiation of antipsychotics begins for nursing home residents and suggesting that nursing homes play an important role in initiation based on a study in Iowa).

way of managing nursing home residents with fewer staff.[283] It was the perfect partnership, and antipsychotics were, and are, being prescribed off-label to control the psychological and behavioral symptoms of dementia in nursing home patients, despite the increased risk of mortality associated with such use.[284] The risks posed by antipsychotics for older patients are so high that nursing homes have federal reporting about the number of residents taking these drugs.[285] Since the government does not publicly report the use of antipsychotics to treat schizophrenia, Huntington's disease, and Tourette's syndrome though, a loophole exists that results in an increasing number of nursing home residents with an unsubstantiated diagnosis for these diseases.[286]

5. Failure to Reset Customary Practice

Once patterns of prescribing have been established, they can be difficult to alter, even when marketing activities formally cease. There are several reasons for this. From the corporate side, informal marketing may continue. When the fines involved in settling lawsuits for off-label marketing are dwarfed by the sales revenue from off-label sales, off-label marketing becomes a viable, albeit illegal, marketing strategy.

From the prescriber side, professional custom is established, and it may be difficult to alter without addressing prescriber misperceptions about Zyprexa and the nursing home staffing shortages that fueled Zyprexa's use. Even after the lawsuits against Eli Lilly for off-label marketing were settled, and federal government programs were established to reduce use of antipsychotics in nursing homes, Zyprexa and other atypical antipsychotics continued to be used in nursing homes, though at lower rates.[287] Rates of

283. Thomas et al., *supra* note 232.

284. *See, e.g.*, Zhang et al., *supra* note 282; Pravin Kamble, Hua Chen, Jeff Sherer & Rajender R. Aparasu, *Antipsychotic Drug Use Among Elderly Nursing Home Residents in the United States*, 6 AM. J. GERIATRIC PHARMACOTHERAPY 187, 188, 195 (2008).

285. Thomas et al., *supra* note 232.

286. *Id.*

287. *See* Ina Jaffe, *Risky Antipsychotic Drugs Still Overprescribed in Nursing Homes*, NPR (Feb. 5, 2018, 8:51 PM), https://www.npr.org/sections/health-shots/2018/02/05/583435517/risky-antipsychotic-drugs-still-overprescribed-in-nursing-homes [https://perma.cc/X2BK-MGUF]; CHRISTI A. GRIMM, OFF. OF THE INSPECTOR GEN., U.S. DEP'T OF HEALTH & HUM.

prescribing antipsychotics for dementia increased at the start of the COVID-19 pandemic, indicating these drugs may still be viewed as a means of treating the symptoms of dementia and addressing staffing shortages.[288] There are also concerns that, with atypical antipsychotics, nursing homes may have simply substituted one class of antipsychotic drugs for another to achieve the same long-standing goals of patient management.[289]

C. Aduhelm: Commercially Engineered Push to Approve a New Alzheimer's Treatment

Alzheimer's disease is a complex, degenerative mental disease with no existing cure and no treatment capable of more than temporarily alleviating symptoms or slowing disease progression.[290] In 2021, an estimated 6.2 million Americans were living with Alzheimer's, and that number could rise to 13.8 million by 2060, in the absence of effective treatments.[291] The total health care costs attributable to Alzheimer's were estimated to be 305 billion dollars in 2020, with much of the expense borne by Medicare and Medicaid.[292] The annual cost of care is projected to reach just under one trillion dollars by 2050.[293] As the U.S. population ages, the disease

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SERVS., OEI-07-20-00500, LONG-TERM TRENDS OF PSYCHOTROPIC DRUG USE IN NURSING HOMES 9, 15 (2022), https://oig.hhs.gov/oei/reports/OEI-07-20-00500.pdf [https://perma.cc/B65Q-2BFK].

288. Hao Luo, Wallis C. Y. Lau, Yi Chai, Carmen Olga Torre, Robert Howard, Kathy Y. Liu, Xiaoyu Lin, Can Yin, Stephen Fortin, David M. Kern, Dong Yun Lee, Rae Woong Park, Jae-Won Jang, Celine S. L. Chui, Jing Li, Christian Reich, Kenneth K. C. Man & Ian C. K. Wong, *Rates of Antipsychotic Drug Prescribing Among People Living with Dementia During the COVID-19 Pandemic*, 80 JAMA PSYCHIATRY 211, 216, 218 (2023).

289. *See* Lisa O'Mary, *Concerns Persist that Nursing Homes May Be Drugging Dementia Patients*, WEBMD (Nov. 18, 2022), https://web.archive.org/web/20240303034416/https://www.webmd.com/a-to-z-guides/news/20221120/concerns-persist-that-nursing-homes-may-be-drugging-dementia-patients [https://perma.cc/S2J3-YQKM]; GRIMM, *supra* note 287.

290. *See, e.g.*, *How Is Alzheimer's Disease Treated?*, NIH: NAT'L INST. ON AGING (Sept. 12, 2023), https://www.nia.nih.gov/health/alzheimers-treatment/how-alzheimers-disease-treated [https://perma.cc/EX9T-9DYB].

291. *2021 Alzheimer's Disease Facts and Figures*, 17 ALZHEIMER'S & DEMENTIA: J. ALZHEIMER'S ASS'N 327, 338, 345 (2021).

292. Winston Wong, *Economic Burden of Alzheimer Disease and Managed Care Considerations*, 26 AM. J. MANAGED CARE S177, S178 (2020) (reporting that Medicare and Medicaid are estimated to cover around 68 percent of the 305 billion dollars in direct health care costs based on 2020 numbers).

293. *2023 Alzheimer's Disease Facts and Figures*, 19 ALZHEIMER'S & DEMENTIA: J.

burden and associated health care costs of Alzheimer's continue to escalate, fueling the demand for treatment that might alleviate the effects of the disease, even if insignificantly.

Despite decades of research, scientists still do not fully understand what causes Alzheimer's disease or how best to treat it. They continue to identify and to study some of its biological features, such as brain plaques and tangles, as well as to explore a variety of avenues to detect, delay, or prevent the onset of disease and to treat its symptoms.[294] Until recently, existing treatments failed to change the underlying disease process and only mitigated some of its symptoms.[295]

It is against this backdrop that on June 7, 2021, the drug aducanumab (trade name Aduhelm), manufactured by U.S. biotechnology company Biogen, received accelerated FDA approval for the treatment of Alzheimer's.[296] At that time, Aduhelm was priced at $56,000 per year; by December of 2021, the price was lowered to $28,200.[297] The FDA approved Aduhelm despite opposition from a council of senior FDA officials and its advisory committee of outside experts, who questioned whether the drug could benefit patients and raised concerns about the risks of taking the drug.[298] Although the controversy surrounding the approval of Aduhelm and its high price tag slowed its adoption by prescribers and payors, Biogen

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ALZHEIMER'S ASS'N, 1598, 1655 (2023).

294. *Alzheimer's Disease Fact Sheet*, NIH: NAT'L INST. ON AGING (Apr. 5, 2023), https://www.nia.nih.gov/health/alzheimers-and-dementia/alzheimers-disease-fact-sheet [https://perma.cc/PSR2-A755].

295. *Id.*

296. Press Release, FDA, FDA Grants Accelerated Approval for Alzheimer's Drug (June 7, 2021), https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-drug [https://perma.cc/N8AW-7FWE].

297. STAFFS OF H. COMM. ON OVERSIGHT & REFORM & H. COMM. ON ENERGY & COM., 117TH CONG., THE HIGH PRICE OF ADUHELM'S APPROVAL: AN INVESTIGATION INTO FDA'S ATYPICAL REVIEW PROCESS AND BIOGEN'S AGGRESSIVE LAUNCH PLANS 13 (2022) [hereinafter HIGH PRICE OF ADUHELM].

298. *See* Rachel Sachs, *The FDA's Approval of Aduhelm: Potential Implications Across a Wide Range of Health Policy Issues and Stakeholders*, HEALTH AFFS. (June 10, 2021), https://www.healthaffairs.org/content/forefront/fda-s-approval-aduhelm-potential-implications-across-wide-range-health-policy-issues [https://perma.cc/KX8G-MUJE]; Pam Belluck, Sheila Kaplan & Rebecca Robbins, *How an Unproven Alzheimer's Drug Got Approved*, N.Y. TIMES (Oct. 20, 2021), https://www.nytimes.com/2021/07/19/health/alzheimers-drug-aduhelm-fda.html [https://perma.cc/U5SN-5NVJ].

continued to overcome hurdles to adoption.[299] In addition, Biogen received accelerated approval for a second drug to treat Alzheimer's disease, a drug in the same class as Aduhelm called Leqembi, based on the results of early-stage studies.[300]

To secure as large a market as possible for Aduhelm, Biogen had to ensure that it became customary care for patients with Alzheimer's disease and possibly other forms of dementia. Biogen's strategy for reaching this goal had multiple prongs, including from the outset: (1) working with the FDA to obtain FDA approval of Aduhelm for the treatment of Alzheimer's disease and negotiating a broad label that includes as many patient groups as possible; (2) encouraging patients, their families and caregivers, and patient advocacy groups to demand access to the drug from prescribers and payors; (3) obtaining coverage of the drug from Medicare, Medicaid, and the U.S. Department of Veterans Affairs (VA); and (4) educating doctors about the benefits of the drug. Biogen's efforts focused on increasing use of the drug by promoting it as the best practice in patient treatment and thereby deserving of insurance reimbursement and broad physician use.

1. Biogen Collaborates with FDA on Drug Approval and Negotiates the FDA Label for Aduhelm

> *[W]ith respect to unknown side-effects of properly prepared products, such as pharmaceuticals ... the risk falls on the user, as long as adequate warnings are provided.*[301]
>
> —Richard A. Epstein

As discussed in Part I, while FDA approval of a drug does not establish professional custom, it provides strong evidence that using

299. *See* Belluck et al., *supra* note 298.

300. *See* Press Release, FDA, FDA Grants Accelerated Approval for Alzheimer's Disease Treatment (Jan. 6, 2023), https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-disease-treatment [https://perma.cc/3CUF-UU9T] ("Leqembi was approved using the Accelerated Approval pathway, under which the FDA may approve drugs for serious conditions where there is an unmet medical need and a drug is shown to have an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit to patients.").

301. Epstein, *supra* note 24, at 582.

the drug for its prescribed purpose conforms with accepted medical treatment practices.[302] It also allows the corporation to market the drug to both physicians and patients for its approved uses.[303] Thus, the easiest way for a corporation to expand its market for a new drug is to obtain, particularly on an expedited basis, FDA approval for a broad indication or range of indications in a large patient group and a label with limited restrictions on use.

In the case of Aduhelm, the path to securing FDA approval was fraught with challenges arising from poor results in clinical testing,[304] but the unusual degree of collaboration between Biogen and the FDA led to ultimate approval.[305] Like earlier drugs targeting amyloid plaques, Biogen's 2015 phase three clinical trials did not appear to provide any measurable benefits.[306] In March 2019, Biogen halted its two partially complete clinical trials based on poor results.[307] But after conversations between Biogen's Head of Research and Development (R&D) and the Director of the FDA's Office of Neuroscience (ON), instead of Biogen abandoning its efforts, in an atypical step, Biogen and the FDA formed a collaborative working group to explore the data and consider avenues for securing approval of Aduhelm.[308] In fact, the ON Director became an advocate for the drug in subsequent FDA proceedings.[309] According to a congressional report investigating irregularities in the FDA process that led to Aduhelm's ultimate accelerated approval, "the FDA-Biogen working group engaged in at least 115 meetings, calls, and substantive email discussions over the course of a year, from July 2019 to July 2020, including convening more than 40 meetings to guide Aduhelm's potential approval."[310]

Biogen submitted an application for a new drug to the FDA in July 2020, based on an unconventional argument that the data from combined trials showed a measurable decline in amyloid plaques for

302. *See supra* Part I.B.
303. *See supra* Part I.B.1.
304. *See* Belluck et al., *supra* note 298.
305. *See id.*
306. Sachs, *supra* note 298.
307. *Id.*
308. HIGH PRICE OF ADUHELM, *supra* note 297, at 8-9.
309. Sachs, *supra* note 298.
310. HIGH PRICE OF ADUHELM, *supra* note 297, at 1.

a subset of enrolled patients.[311] In another departure from the normal review process, Biogen and the FDA worked together for several months on a joint briefing document prepared for the FDA's Peripheral and Central Nervous System (PCNS) Advisory Committee to support Biogen's application for drug approval.[312] On November 6, 2020, the FDA held a meeting of the relevant expert advisory committee to review the evidence about the clinical efficacy of the drug, and the committee voted overwhelmingly that the evidence did not establish evidence of the drug's effectiveness.[313]

Although it is not required to do so, the FDA generally follows its advisory committee's recommendations, but this time it radically departed from the committee.[314] In April 2021, the FDA made the unusual move of pivoting from the traditional approval pathway to an accelerated pathway program.[315] This program enables the FDA to approve a drug for a serious or life-threatening disease based on a surrogate endpoint that is reasonably likely to predict clinical benefit, rather than requiring a showing of actual health benefit.[316] The FDA determined that the surrogate endpoint was the reduction of amyloid beta plaque rather than clinical benefit.[317]

On June 7, 2021, the FDA approved the drug pursuant to the accelerated pathway program.[318] In the FDA's press release, Aduhelm was heralded as "the first new treatment approved for Alzheimer's since 2003" and "the first therapy to target and affect the underlying disease process," rather than simply treating symptoms of the disease.[319] The FDA approved a very broad label for the drug that stated simply that the drug is indicated "for the treatment of Alzheimer's disease" without further restriction.[320]

311. Press Release, Biogen, Biogen Completes Submission of Biologics License Application to FDA for Aducanumab as a Treatment for Alzheimer's Disease (July 8, 2020), https://investors.biogen.com/news-releases/news-release-details/biogen-completes-submission-biologics-license-application-fda [https://perma.cc/DEA6-E5C6].

312. HIGH PRICE OF ADUHELM, *supra* note 297, at 1-2.

313. *See id.* at 9-10.

314. *See id.* at 9.

315. *See id.* at 4, 11.

316. *See* U.S. FOOD & DRUG ADMIN., OMB CONTROL NO. 0910-0765, GUIDANCE FOR INDUSTRY: EXPEDITED PROGRAMS FOR SERIOUS CONDITIONS—DRUGS AND BIOLOGICS 6-7 (2014).

317. HIGH PRICE OF ADUHELM, *supra* note 297, at 12.

318. *Id.* at 11.

319. Press Release, FDA, *supra* note 296.

320. *Aduhelm Label*, FDA (June 2021), https://www.accessdata.fda.gov/drugsatfda_docs/

Because the FDA approved the drug on the basis of its effect in reducing amyloid beta plaque, it reasoned that this reduction could benefit patients at all stages of the disease.[321] This broad label allowed Biogen to engage in direct marketing of the drug to prescribers and patients as well as to create some level of comfort among prescribers that the drug could be used broadly (and perhaps drive pressure on them to prescribe it broadly), without clinical proof.[322] Pursuant to the accelerated pathway program, Biogen is required to complete post-marketing studies over nine years—while Aduhelm is on the market—to confirm its anticipated clinical benefit.[323] The overall track record for corporate compliance with the post-marketing requirements of the accelerated approval pathway is poor, though, and few drugs are withdrawn even when there is no evidence of clinical benefit.[324]

Meanwhile, Aduhelm has some significant risks, including potential brain swelling (amyloid related imaging abnormalities (ARIA)) and risk of hypersensitivity reactions.[325] Indeed, safety data from clinical trials of the drug showed that 41 percent of patients in key clinical trials experienced brain bleeding or swelling.[326] Yet, at first Aduhelm was approved for patients at risk for ARIA with only an FDA label warning about the serious risks associated with the

label/2021/761178s000lbl.pdf [https://perma.cc/4FGF-7DYM]; Andrew Joseph, *An Extra Twist in the FDA's Alzheimer's Decision: No Limits on Which Patients Can Get the Drug*, STAT (June 7, 2021), https://www.statnews.com/2021/06/07/twist-fda-alzheimers-decision-no-limits-on-patients/ [https://perma.cc/2NRG-2E9X].

321. Joseph, *supra* note 320; *see also* Adam Feuerstein & Damian Garde, *FDA Grants Historic Approval to Alzheimer's Drug Designed to Slow Cognitive Decline*, STAT (June 7, 2021), https://www.statnews.com/2021/06/07/fda-grants-historic-approval-to-alzheimers-drug-designed-to-slow-cognitive-decline/ [https://perma.cc/JJF2-3QVN].

322. *See* HIGH PRICE OF ADUHELM, *supra* note 297, at 41. *See generally* Joseph, *supra* note 320.

323. HIGH PRICE OF ADUHELM, *supra* note 297, at 12.

324. *See* OFF. OF THE INSPECTOR GEN., U.S. DEP'T OF HEALTH & HUM. SERVS., OEI-01-21-00401, DELAYS IN CONFIRMATORY TRIALS FOR DRUG APPLICATIONS GRANTED FDA'S ACCELERATED APPROVAL RAISE CONCERNS 1-3 (Sept. 29, 2022), https://oig.hhs.gov/oei/reports/OEI-01-21-00401.asp [https://perma.cc/JM78-UJ3Q]. The FDA's approval of Aduhelm raised concerns about the accelerated approval pathway, resulting in a subsequent study by OIG and the publication of a report. *See id.* at 1.

325. *See Aduhelm Label*, *supra* note 320; *see also* Pam Belluck, *Concerns Grow over Safety of Aduhelm After Death of Patient Who Got the Drug*, N.Y. TIMES (Nov. 22, 2021), https://www.nytimes.com/2021/11/22/health/aduhelm-death-safety.html [https://perma.cc/XL68-JY7U].

326. Belluck, *supra* note 325.

drug.[327] The label also called for less frequent monitoring than was required during the clinical trials, despite the American Academy of Neurology suggesting that "additional MRIs will often be needed in response to changes in patients' clinical condition."[328] While the drug remained widely available, the label was subsequently modified to reflect the limited data on effectiveness, now stating that "[t]reatment with ADUHELM should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials."[329]

2. Biogen and Eisai Work with Patients and Patient Groups to Generate Demand

Pharmaceutical companies have long engaged patient advocacy groups and patients themselves in efforts to encourage use of their drugs.[330] Once approved, Biogen, along with its co-developer and collaborator, Eisai, invested extensively in generating demand for the drug from patients, their caregivers, and patient advocacy organizations.[331] They also engaged in actions to remove financial barriers to accessing the drug, which is priced at $28,200 per year.[332]

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327. *See id.*

328. Winston Chiong, Benjamin David Tolchin, Richard J. Bonnie, Katharina M. Busl, Salvador Cruz-Flores, Leon G. Epstein, Ericka P. Greene, Judy Illes, Matthew Kirschen, Daniel G. Larriviere, Sneha Mantri, Michael A. Rubin, Barney J. Stern & Lynne P. Taylor, *Decisions with Patients and Families Regarding Aducanumab in Alzheimer Disease, with Recommendations for Consent: AAN Position Statement*, 98 NEUROLOGY 154, 156 (2022).

329. Press Release, Biogen, FDA Approves Updated ADUHELM™ Prescribing Information to Emphasize Population Studied in Clinical Trials (July 8, 2021) (emphasis omitted), https://investors.biogen.com/news-releases/news-release-details/fda-approves-updated-aduhelmtm-prescribing-information-emphasize [https://perma.cc/9HMR-J6F9].

330. *See* So-Yeon Kang, Ge Bai, Laura Karas & Gerard F. Anderson, *Pharmaceutical Industry Support of US Patient Advocacy Organizations: An International Context*, 109 AM. J. PUB. HEALTH 559, 559-60 (2019). *See generally* BD. ON HEALTH SCIS. POL'Y, CONFLICT OF INTEREST IN MEDICAL RESEARCH, EDUCATION, AND PRACTICE (Bernard Lo & Marilyn J. Field eds., 2009).

331. *See* Press Release, Biogen, Biogen and Eisai Launch Multiple Initiatives to Help Patients with Alzheimer's Disease Access ADUHELM™ (June 7, 2021), https://investors.biogen.com/news-releases/news-release-details/biogen-and-eisai-launch-multiple-initiatives-help-patients [https://perma.cc/HQD5-3P33].

332. Press Release, Biogen, Biogen Announces Reduced Price for ADUHELM® to Improve Access for Patients with Early Alzheimer's Disease (Dec. 20, 2021), https://investors.biogen.com/news-releases/news-release-details/biogen-announces-reduced-price-aduhelmr-improve-access-patients [https://perma.cc/4X2L-XWCW].

Given the dearth of good options for treating Alzheimer's disease, Aduhelm seemed to offer a ray of hope for many desperate patients, and Biogen invested in developing and expanding its relationships with patient advocacy groups and marketing efforts directed at prescribers, patients, and caregivers.[333] Biogen developed relationships and provided financial support to a number of patient advocates, such as the Alzheimer's Association, to seek approval for the drug and then to pressure physicians for the drug once approved.[334] The Alzheimer's Association, with Biogen funding, waged an expensive advocacy campaign prior to the FDA's decision designed to encourage approval called the "More Time" campaign.[335] This campaign engaged celebrities and was designed to build grassroots support for approval of the drug.[336]

These efforts paid off. Physicians are often encouraged to prescribe Aduhelm by patients and patient families desperate for treatment.[337] One physician suggests that private practice physicians may be more likely to prescribe Aduhlem than academic scientists, who hesitate to do so after looking at the scientific data.[338]

While Aduhelm's cost could deter demand, patients have few choices, and many patients are insured by either Medicare or private group plans. Additionally, immediately after FDA approval, Biogen announced a range of programs designed to provide education about and access to the drug to qualified patients, laying the

333. *See, e.g.*, Michael S. Sinha & Stephen Latham, *Patient Advocacy Organizations and FDA Drug Approval: Lessons from Aduhelm*, STAT (July 23, 2021), https://www.statnews.com/2021/07/23/patient-advocacy-organizations-lessons-from-aducanumab/ [https://perma.cc/7FTY-LCYC].

334. Beth Snyder Bulik, *Aduhelm Reignites Questions Around Ties Between Pharma and Patient Advocacy Orgs*, ENDPOINTS NEWS (Feb. 8, 2022, 1:02 PM), https://endpts.com/aduhelm-reignites-questions-around-ties-between-pharma-and-patient-advocacy-orgs/ [https://perma.cc/H49B-LNYS].

335. *See* Beth Snyder Bulik, *Celeb-Backed Alzheimer's Association Campaign Aims to Build Grassroots Support for Biogen's Aducanumab Ahead of FDA Decision*, FIERCE PHARMA (May 14, 2021, 11:22 AM), https://www.fiercepharma.com/marketing/alzheimer-s-association campaign-more-time-supports-biogen-s-aducanumab-awaiting-fda [https://perma.cc/SM9K-E2QD].

336. *See id.*

337. *See* Beth Snyder Bulik, *Ready, Set, Prescribe? Doctors Detail Why They'll Deploy Biogen's New Alzheimer's Drug—or Not*, FIERCE PHARMA (June 8, 2021, 7:40 AM), https://www.fiercepharma.com/marketing/biogen-s-alzheimer-s-drug-aduhelm-approved-patients-demand-skyrockets-and-physicians-prep [https://perma.cc/9LS6-LP3F].

338. *See id.*

foundation for robust patient demand despite the drug's high cost.[339] When faced with uncertainty about whether Medicare would pay for Aduhelm, Biogen sought to grow demand by offering the treatment free-of-charge to select patients.[340] Other initiatives to address financial barriers to accessing Aduhelm included joint programs with the National Association of Free and Charitable Clinics and CVS Health as well as efforts to negotiate a multi-year agreement with the Veterans Health Administration (VHA).[341] As described by Biogen, "[t]hese initiatives aim to help patients and their families understand the disease, navigate the diagnostic journey, secure culturally competent care and afford treatment."[342]

3. Biogen "Educates" Doctors About Drug's Benefits

Part of generating demand for a drug entails seeking, and then using, a broad FDA drug label to promote evidence-based uses by physicians. The FDA plays a central role in the practice of evidence-based prescribing by requiring scientific and medical evidence of safety and efficacy of new drugs as a condition of approval to sell the drugs on the market.[343] Physicians and the public consider FDA approval of a drug as a reliable signal that the drug is likely to provide benefits that outweigh known and potential risks for its approved uses for an intended population.[344] Thus, while FDA approval does not itself establish professional custom, it plays an

339. *See* Press Release, Biogen, *supra* note 331.

340. *See* Deena Beasley, *Focus: Biogen Offers Free Alzheimer's Drug as Medicare Payment Uncertainty Remains*, REUTERS (Aug. 30, 2021, 3:57 PM), https://www.reuters.com/world/us/biogen-provides-free-aduhelm-us-clinics-await-medicare-payment-2021-08-30/ [https://perma.cc/7PG7-N96M].

341. *ADUHELM (aducanumab-avwa) for the Treatment of Alzheimer's Disease*, CLINICAL TRIALS ARENA (July 13, 2021), https://www.clinicaltrialsarena.com/projects/aduhelm-aducanumab-avwa-alzheimers/ [https://perma.cc/4PK3-YEYK].

342. *See* Press Release, Biogen, *supra* note 331 (discussing Biogen's advertisements of its patient initiatives).

343. *But see, e.g.*, Donald W. Light, *Serious Risks and Few New Benefits from FDA-Approved Drugs*, HEALTH AFFS. (July 6, 2015), https://www.healthaffairs.org/content/forefront/serious-risks-and-few-new-benefits-fda-approved-drugs [https://perma.cc/2BWC-VHFA] (arguing that industry influence over the FDA approval process turns clinical guidelines into marketing tools).

344. *See* Rebecca Dresser & Joel Frader, *Off-Label Prescribing: A Call for Heightened Professional and Government Oversight*, 37 J.L. MED. & ETHICS 476, 477 (2009).

important role in physician decisions about whether and when to use a drug, which helps to establish customary use of the drug.

While physicians can prescribe a drug for uses beyond those indicated on the drug label, the FDA approval process offers them some comfort that the approved uses are supported by medical and scientific evidence.[345] After the drug is approved, the manufacturer can engage in a marketing campaign to "educate" physicians about the approved uses of the drug and encourage them to use the drug for those uses. Once the drug is on the market, physicians have the ability, and may build up the comfort, to prescribe the drug for uses beyond those on the label.[346] In some cases, when off-label uses become commonplace, physicians may not even know that they are using the drugs off-label.[347]

While Aduhelm's broad label alone could encourage physicians to prescribe it, Biogen strove to expand broaden physician support for the drug.[348] Biogen invested significant time and money in cultivating physicians as key opinion leaders to support and encourage use of Aduhelm actively, despite its questionable efficacy.[349] Four physicians worked as such paid consultants for Biogen;[350] as disclosed in their articles, they received financial support for publications in scientific journals that promote the clinical benefits of Aduhelm.[351]

345. *See* Teresa Carr, *How Off-Label Prescribing Can Put You at Risk*, CONSUMER REPS. (Feb. 22, 2016), https://www.consumerreports.org/drugs/how-off-label-prescribing-can-put-you-at-risk/ [https://perma.cc/4J39-JL42].

346. *See id.*

347. *Id.*

348. *See* Bulik, *supra* note 335.

349. *See* Nicholas Florko, *The Loudest Physician Proponents of Aduhelm Have All Taken Money From Biogen*, STAT (Nov. 1, 2021), https://www.statnews.com/2021/11/01/the-loudest-physician-proponents-of-aduhelm-have-all-taken-money-from-biogen/ [https://perma.cc/VMP4-6J2M].

350. *Id.*

351. *See, e.g.*, Jeffrey Cummings, Paul Aisen, Cynthia Lemere, Alireza Atri, Marwan Sabbagh & Stephen Salloway, *Aducanumab Produced a Clinically Meaningful Benefit in Association with Amyloid Lowering*, 13 ALZHEIMER'S RSCH. & THERAPY 1, 1-3 (2021).

4. Biogen Fights to Secure Reimbursement for Aduhelm from Government-Sponsored Health Programs

Once patients and physicians sought to obtain Aduhelm, Biogen needed to secure insurance coverage for it. Payors also play a role in determining whether an approved drug becomes widely prescribed. Where the price tag of a drug is high, as is true for many new drugs, patients may not be able to afford the drug without coverage from government or private insurance.

Given the older demographic affected by Alzheimer's, coverage by Medicare is particularly important to ensure widespread adoption of Aduhelm. In 2003, Medicare coverage was expanded to include Part D plans that provide coverage of outpatient prescription drugs, providing significant financial support to patients who might not otherwise be able to access expensive prescription drugs.[352] Since that expansion of Medicare, securing a place on Part D formularies has become a critical part of pharmaceutical marketing strategies to expand prescription drug utilization, particularly for drugs such as Aduhelm, which is marketed to patients over age sixty-five.[353] Typically, securing a place on the formulary is routine for a drug that receives FDA approval, and drug companies have thus largely focused their attention on improving their relationship with the FDA.[354] Yet in an unprecedented move, and amidst controversy and opposition from drug companies, patient advocacy groups, and some Republican lawmakers,[355] on April 7, 2022, CMS announced its final decision to restrict Medicare coverage of Aduhelm to patients enrolled in clinical trials.[356]

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352. *See* Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, § 101, 117 Stat. 2066, 2071-72 (2003).

353. *See* Darius Lakdawalla, Neeraj Sood & Qian Gu, *Pharmaceutical Advertising and Medicare Part D*, 32 J. HEALTH ECON. 1356, 1356, 1366 (2013).

354. Arthur Allen & Kaiser Health News, *Inside the Lobbying Push to Get Medicare to Pay for a Controversial Alzheimer's Drug*, FORTUNE (Feb. 16, 2022, 5:24 PM), https://fortune.com/2022/02/16/aduhelm-alzheimers-drug-medicare-coverage/ [https://perma.cc/R9TW-B4VT].

355. *Id.*

356. *See* Press Release, Ctrs. for Medicare & Medicaid Servs., CMS Finalizes Medicare Coverage Policy for Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (Apr. 7, 2022), https://www.cms.gov/newsroom/press-releases/cms-finalizes-medicare-coverage-policy-monoclonal-antibodies-directed-against-amyloid-treatment [https://perma.cc/XZ3A-NXK5]; *see also* Gretchen Jacobson & Aimee Cicchiello, *Medicare's Decision to Cover the Alzheimer's Drug Aduhelm: What Will It Mean for Patients and the*

In response to Medicare's decision to limit coverage, Biogen, along with patient advocacy groups such as UsAgainstAlzheimer's, expanded their lobbying presence to reverse Medicare's decision.[357] Biogen also likely considered legally challenging the CMS coverage decision.[358] Despite continuing pressure from industry, as well as from some members of Congress,[359] CMS decided to enforce its limited coverage decision for Aduhelm and to extend it to Leqembi.[360] CMS stated that "Medicare will cover drugs with traditional FDA approval when a physician and clinical team participates in the collection of evidence about how these drugs work in the real world, also known as a registry."[361]

Biogen also worked with the VHA to try to secure coverage of Aduhelm for veterans and qualifying family members.[362] In addition to 360,000 family beneficiaries of varying ages,[363] the VHA has about nine million enrolled veterans, almost half of whom are over the age of sixty-five, a huge market for Aduhelm.[364] The VA ultimately

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Program?, COMMONWEALTH FUND (Apr. 8, 2022), https://www.commonwealthfund.org/blog/2022/medicares-decision-cover-alzheimers-drug-aduhelm-what-will-it-mean-patients-and-program [https://perma.cc/5JM6-CSEH].

357. *See* Katherine Ellen Foley & Megan Wilson, *'Not a Tolerable Situation': Patient Groups Take Aim at CMS over Alzheimer's Coverage Decision*, POLITICO (Jan. 17, 2022, 7:00 AM), https://www.politico.com/news/2022/01/17/alzheimers-coverage-patient-groups-cms-527170 [https://perma.cc/4GYX-KELC].

358. *See* Angus Liu, *Biogen Brings an Unlikely Lobbyist into Its Alzheimer's Corner. Could a CMS Challenge Follow?*, FIERCE PHARMA (Apr. 21, 2022, 10:00 AM), https://www.fiercepharma.com/pharma/biogen-hired-congress-leaders-relative-alzheimers-drug-lobbying-work-amid-aduhelms-cms [https://perma.cc/X9JP-DTL9].

359. Rachel Cohrs Zhang, *Medicare Holds Firm on Alzheimer's Drug Coverage Policy*, STAT (June 1, 2023), https://www.statnews.com/2023/06/01/medicare-alzheimers-drug-policy/ [https://perma.cc/T8Z8-YMDG].

360. Peter Wehrwein, *CMS Sticks to Sharply Limited Coverage of New Alzheimer's Drug, Leqembi*, MANAGED HEALTHCARE EXEC. (Feb. 23, 2023), https://www.managedhealthcareexecutive.com/view/cms-sticks-to-sharply-limited-coverage-of-new-alzheimer-s-drug-leqembi [https://perma.cc/V9TL-Z6Y9].

361. Press Release, Ctrs. for Medicare & Medicaid Servs., CMS Announces Plan to Ensure Availability of New Alzheimer's Drugs (June 1, 2023), https://www.cms.gov/newsroom/press-releases/cms-announces-plan-ensure-availability-new-alzheimers-drugs [https://perma.cc/6YG3-VRHD].

362. *See* Press Release, Biogen, *supra* note 331.

363. *Information for Family Members and Dependents*, U.S. DEP'T VETERANS AFFS., https://www.va.gov/COMMUNITYCARE/programs/dependents/index.asp [https://perma.cc/7RXV-ECFF].

364. *See* Press Release, Biogen, *supra* note 331.

declined to cover Aduhelm broadly, recommending against including the drug in its updated prescription drug formulary.[365]

While engaging in the development and marketing of Aduhelm, Eisai and Biogen were simultaneously pursuing the development and commercialization of a similar drug, Leqembi, which received accelerated approval from the FDA in January 2023, and full approval in July 2023.[366] The CMS restrictions on reimbursement were removed once Leqembi received full approval.[367] While appearing safer than Aduhelm, Leqembi seems to offer small to uncertain benefits and brings with it safety risks and high costs.[368] Biogen announced its decision to discontinue the commercialization of Aduhelm and focus solely on the commercialization of Leqembi on January 31, 2024.[369] Biogen is now working on increasing sales of Leqembi, including a 30 percent increase in its U.S. sales force designed to drive up sales of its drugs.[370]

In summary, this case study shows the ways in which industry influence drives government approval of a drug (or now two drugs) with little benefit, harmful side effects, and a high cost.[371] It also demonstrates the pathways of influence over patients, physician

365. *See* Ned Pagliarulo, *VA Leaves Aduhelm Off Coverage List, Recommending Against Controversial Alzheimer's Drug*, BIOPHARMA DIVE (Aug. 12, 2021), https://www.biopharmadive.com/news/va-aduhelm-formulary-coverage-alzheimers/604884/ [https://perma.cc/29LZ-FAAJ].

366. *See* Beatriz Ramon, *Leqembi and the Accelerated Approval Pathway*, UPDATE MAG., Spring 2024, at 31, 31.

367. *See* Deena Beasley & Julie Steenhuysen, *US FDA Grants Standard Approval of Eisai/Biogen Alzheimer's Drug*, REUTERS (July 7, 2023, 11:55 AM), https://www.reuters.com/business/healthcare-pharmaceuticals/us-fda-grants-standard-approval-eisaibiogen-alzheimers-drug-2023-07-06/ [https://perma.cc/9V9M-6EW3].

368. *See* Esther Choo, *The New Alzheimer's Drug Is a Step Forward. But It Falls Far Short of a Miracle*, MSNBC (July 10, 2023, 6:06 PM), https://www.msnbc.com/opinion/msnbc-opinion/leqembi-alzheimers-drug-benefits-expectations-rcna93524 [https://perma.cc/GM98-ATD2].

369. *See Biogen Discontinues Aduhelm to Focus on Leqembi for Alzheimer's Disease*, PHARM. TECH. (Feb. 28, 2024), https://www.pharmaceutical-technology.com/analyst-comment/biogen-discontinues-aduhelm-alzheimers/ [https://perma.cc/5M46-E6LR].

370. *See* Nick Paul Taylor, *Biogen Plots 30% Leqembi Field Force Bump, Omnichannel Campaigns as Launch Enters New Phase*, FIERCE PHARMA (Apr. 25, 2024, 6:58 AM), https://www.fiercepharma.com/marketing/biogen-plots-30-leqembi-field-force-bump-omnichannelcampaigns-launch-enters-new-phase [https://perma.cc/547L-59VC].

371. *See* Sam Gandy, *6 Ways the FDA's Approval of Aduhelm Does More Harm than Good*, STAT (June 15, 2021), https://www.statnews.com/2021/06/15/6-ways-fda-approval-aduhelm-does-more-harm-than-good/ [https://perma.cc/SA6V-QUBA].

groups, and public and private payors. Given the scarcity of Alzheimer's treatments, it is likely that as industry efforts persist, use of Leqembi will expand, and it will creep towards customary use, establishing it as the standard of care in at least some states.

III. TOWARD A NEW JURISPRUDENCE FOR NEGLIGENT PRESCRIBING

The case studies in Part II illustrate the corporate pathways of influence that disrupt the professional custom standard for prescribing in tort, reshaping what is considered reasonable care. This is significant because, as our empirical survey shows, custom continues to play a large role in determining liability in medical malpractice cases. When corporations influence what constitutes reasonable care, it disrupts the form and function of the law and undermines patient protection. Given the ability of corporations to affect professional custom, courts must not defer solely to professionals to determine what is reasonable in medical malpractice litigation over prescribing practices.

In this Part, we provide further arguments supporting a doctrinal shift for negligent prescribing—the abandonment of the professional custom standard in favor of a reasonable person standard similar to the one adopted and implemented in seven states.[372] We advocate for a reasonableness standard for prescribing that is responsive to the issues raised by our case studies about industry influence over the legal standard of professional custom and, ultimately, what satisfies the legal standard of care. This shift is supported by both legal and medical practice. We argue that the historical counterarguments marshalled against a reasonableness standard—including judicial and juror incompetence and quality of care concerns—are unsupported and easily refuted, and that the issues they raise are better addressed in modern times by a reasonableness standard.

372. These states are Florida, Maryland, Oregon, Rhode Island, Vermont, Wisconsin, and Wyoming. *See supra* Table 2.

A. Restoring the Form and Function of the Law

Legal and medical practice arguments support a shift from a professional custom standard to a reasonableness standard for negligent prescribing. Shifting to a reasonableness standard would restore the form and function of the law by resolving confusion in the courts about the proper evidentiary scope to determine breach and by creating opportunities to address the corporate distortion of professional practice.

The role of professional custom is muddled, as some states do not have a clear approach, others adopt professional custom but examine evidence outside that realm, and yet others adopt a reasonableness test but rely heavily on evidence of professional custom.[373] Shifting to a reasonableness standard would restore a clear approach to determine breach by which evidence of professional custom is probative but not dispositive. It also would allow courts to consider a broader range of evidence of reasonable practice, mitigating corporate influence on professional practice.

This shift to a reasonableness standard could have a significant impact on medical malpractice litigation, as professional custom continues to play a large role in resolving malpractice claims, including those involving prescribing practices. Recall that twelve states adopt and follow a professional custom standard to determine breach.[374] Twenty-three states have an unclear standard, where professional custom may play a dominant role, and one state (Louisiana) has explicitly adopted a hybrid standard.[375] Fourteen states appear to adopt a reasonableness test, but the jurisprudence in only seven of those states—Florida, Maryland, Oregon, Rhode Island, Vermont, Wisconsin, and Wyoming—appeals to more than professional custom to resolve medical malpractice claims.[376] And even among these states, there is some ambiguity about whether evidence outside professional custom is given equal weight.[377] Shifting to a reasonableness standard would clarify the role of

373. *See supra* Part I.C.2.
374. *See supra* Table 1.
375. *See supra* Table 1.
376. *See supra* Tables 1-2.
377. *See* Satz & Vertinsky, *supra* note 111.

professional custom as only one possible part of a reasonableness inquiry. Custom would not be determinative but probative information for a jury to consider. For example, in Florida, "[t]he fact that a person deviates from or conforms to an accepted custom or practice does not establish conclusively that the person was or was not negligent."[378]

Understanding professional custom as part of a reasonableness test is also significant because it helps to clarify the role of professional custom historically. Notably, it sheds new light on earlier cases viewed as aberrations, such as *Helling v. Carey*, which found negligence when professional custom was followed.[379] Because this case involved the failure to provide an inexpensive glaucoma test, it is often discussed as resting on an implicit cost-benefit analysis.[380] Commentators suggest that this case represents judicial confusion about the benefits of choosing a cost-benefit analysis over professional custom to determine medical malpractice.[381] But this case may instead be an example of the benefits of a court having the latitude to respond to harmful customary practice. Understood in this way, *Helling v. Carey* was an early recognition of the need to look beyond professional custom to protect patients from harm. As the court stated:

> Under the facts of this case reasonable prudence required the timely giving of the pressure test to this plaintiff. The precaution of giving this test to detect the incidence of glaucoma to patients under 40 years of age is so imperative that irrespective of its disregard by the standards of the ophthalmology profession, it is the duty of the courts to say what is required to protect patients under 40 from the damaging results of glaucoma.[382]

In practice, a shift to a reasonableness standard would broaden the scope of evidence in medical malpractice cases. In addition to evidence of professional custom through testimony and written

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378. Nesbitt v. Cmty. Health of S. Dade, Inc., 467 So. 2d 711, 714 (Fla. Dist. Ct. App. 1985).

379. *See* 519 P.2d 981, 983 (Wash. 1974) (en banc).

380. *See id.*

381. *See, e.g.*, Richard A. Epstein, *The Path to* The T. J. Hooper*: The Theory and History of Custom in the Law of Tort*, 21 J. LEGAL STUD. 1, 3, 37 (1992) (discussing *Helling*).

382. *Helling*, 519 P.2d at 983.

documents, courts could look to practice guidelines, reimbursement policies, and other sources to determine best practices. This has a couple of important implications. It would provide greater opportunities to address the ability of corporations to influence the legal standard for professional custom through the pathways of influence discussed in Part II.[383] Additionally, it would allow challenges to customs that cause patient harm. This not only protects patients but also supports health care practitioners. It shields practitioners from liability for failing to follow harmful professional customs. It also creates an environment for innovation that allows best practices to evolve.

This would not be the first time in history that courts sought to broaden the scope of evidence in medical malpractice cases beyond professional custom to promote fairness between physicians and patients. The twentieth century saw the abandonment of the locality rule in some states, and this shift was tied to a broadened scope of evidence.[384] This is because the rejection of "local custom" in favor of "national custom" carried with it a broader, reasonableness query.[385] Courts that previously looked to what was considered reasonable within a small geographic area were now able to reference national practice trends.

This shift from the locality rule to national custom is part of what muddled the role of professional custom historically. Even though this shift did not require the abandonment of professional custom, once courts embraced a national approach, judicial decisions became less clear about the distinction between "professional custom" and national evidence of acting reasonably within the profession. Some states appeared to implicitly adopt a reasonableness test. In Maryland, for example, a court rejected the locality rule and held that "a physician is under a duty to use that degree of care and skill

383. For additional ideas on how to address this problem, see, for example, David A. Simon, *Off-Label Innovation*, 56 GA. L. REV. 701, 701-02 (2022) (exploring the idea of incentivizing physicians rather than pharmaceutical companies to generate the post-market information needed to inform prescribing off-label).

384. *See* Jon R. Waltz, *The Rise and Gradual Fall of the Locality Rule in Medical Malpractice Litigation*, 18 DEPAUL L. REV. 408, 411-12, 415-18 (1969); *see also* John Kimbrough Johnson, Jr., *An Evaluation of Changes in the Medical Standard of Care*, 23 VAND. L. REV. 729, 733-34 (1970).

385. Philip G. Peters, Jr., *The Quiet Demise of Deference to Custom: Malpractice Law at the Millennium*, 57 WASH. & LEE L. REV. 163, 186-87 (2000).

which is expected of a reasonably competent practitioner in the same class to which he belongs, acting in the same or similar circumstances."[386] Under this standard, Maryland courts suggest looking at a broad range of evidence that may exceed professional custom: "[A]dvances in the profession, availability of facilities, specialization or general practice, proximity of specialists and special facilities, together with *all other relevant considerations*, are to be taken into account."[387]

Rhode Island was more explicit in its reasons for rejecting the locality rule and then adopting a reasonableness test, since professional custom under the locality rule failed to address the potential "conspiracy of silence" amongst physicians about deleterious medical practices.[388] One Rhode Island court explained that "the focus in any medical malpractice case should be the procedure performed and the question of whether it was executed in conformity with the recognized standard of care, *the primary concern being whether the treatment was administered in a reasonable manner*."[389] After rejecting the locality rule, the court held that "a physician is under a duty to use the degree of care and skill that is expected of a reasonably competent practitioner in the same class to which he or she belongs, acting in the same or similar circumstances."[390] "According to the court, [n]o one issue ... should be determinative."[391]

A national move to a reasonableness standard would clarify the role of professional custom as only one type of probative information for a jury or judge to consider. Instead of allowing professional custom to determine breach, courts would evaluate a broader range of evidence. This could help address corporate influence on professional custom, which may create standards that improperly impose liability on physicians and generate patient harm.

386. Shilkret v. Annapolis Emergency Hosp. Ass'n, 349 A.2d 245, 253 (Md. 1975).

387. *Id.* (emphasis added).

388. *See* Sheeley v. Mem'l Hosp., 710 A.2d 161, 165-66 (R.I. 1998) (citing *Shilkret*, 349 A.2d at 249).

389. *Id.* at 166 (emphasis added).

390. *Id.* at 167; *see also* Riley v. Stone, 900 A.2d 1087, 1093 (R.I. 2006).

391. *Sheeley*, 710 A.2d at 166.

B. Addressing Counterarguments

Part I described the historical justifications for the professional custom standard. While none are well-substantiated or particularly compelling, the longevity of the professional custom doctrine requires consideration of these and other possible counterarguments. This section argues that the modern practice of medicine seems better supported by a reasonableness rather than a professional custom standard.

The first category of counterarguments—and likely the strongest—involves concerns about judicial and juror incompetence under a reasonableness standard. Related to this is the argument that medical professionals should be afforded a heightened status, given their special training and unique ability to determine what is in their patients' best interests. To be sure, pharmaceuticals and the technology behind them may be scientific in nature, and questions about their application difficult for a person who is not scientifically trained to understand. But the baseline questions in prescribing cases involve other questions, namely those about informed consent to drug protocols and harms that occur from drug use. A judge or properly instructed jury could determine whether material risks were disclosed to a patient, a patient gave adequate consent, and, based on medical records and other testimony, a patient experienced physical or mental harm.

Even if judicial and juror incompetence about pharmaceuticals remained a concern in some cases, the playing field has shifted, such that courts can no longer trust that professional custom reflects best medical practices from a health outcomes perspective. This has created a new type of incompetence concern, one in which courts may be unaware of the corporate influence on professional custom and the legal standard of reasonable care. Corporate pathways of influence have created new markets for potentially harmful drugs that become part of professional custom.[392] Shifting to a reasonableness test would provide more checks on juror and judicial incompetence about corporate influence because it would allow for a broader range of evidence to establish reasonable medical practice.

392. *See* Elliott, *supra* note 21, at 164-66.

The second set of counterarguments pertains to quality of care issues and involves concerns about the reasonableness standard allowing medical practices that depart from what is most common and thereby harming patients. A related concern is that the reasonableness standard will result in defensive medicine.[393] The argument is that because medical practitioners will be less certain of what is expected of them, they will allow litigation risk rather than their patients' best interests to guide their practice.

This set of counterarguments is turned on its head by the current corporate pathways of influence on professional custom. In the face of industry influence over prescribing, quality of care may not be synonymous with the most common prescribing practices. Further, industry influence on professional custom could itself lead to defensive medicine when prescribers are wary of departing from widely adopted practices. The use of opioids is a poignant example. Corporate-driven demand resulted in opioid overuse and massive waves of addiction and deaths.[394] Then, when professional custom shifted against opioid use in the wake of lawsuits, opioids became unavailable for patients who needed them to manage chronic pain.[395] Neither of these professional customs supports patient health outcomes.

Additionally, there are benefits to a reasonableness standard for the practice of medicine. Adopting a reasonableness test will provide physicians with doctrinal clarity of the tort standard. Further, physicians will not be forced to follow harmful customs or face legal liability.

The last set of counterarguments is about the feasibility of moving toward a reasonableness standard. Litigation could become more complex and prolonged when a broader range of evidence is allowed. But as our empirical survey in Part I shows, under the professional custom standard, jurors are already asked to consider evidence beyond professional practice. There is no indication in these states or the states that have formally moved to a reasonableness standard

393. *See* HARPER ET AL., *supra* note 53, at 583-84 n.6.

394. *See, e.g.*, Vertinsky, *supra* note 16, at 188-89, 191.

395. *See, e.g.*, Christina Jewett & Ellen Gabler, *Opioid Settlement Hinders Patients' Access to a Wide Array of Drugs*, N.Y. TIMES (Mar. 14, 2023), https://www.nytimes.com/2023/03/13/us/drug-limits-adhd-depression.html [https://perma.cc/4T4T-8W7P].

that litigation is made more burdensome by giving professional custom probative rather than dispositive value.

CONCLUSION AND BROADER IMPLICATIONS FOR MEDICAL MALPRACTICE AND THE "LEARNED PROFESSIONS"

This Article argues for the abandonment of the professional custom standard for prescribing practices in tort. In Part I, our survey of professional custom cases demonstrates that while professional custom continues to play an outsized role in medical malpractice litigation—formally or by default—the standard is inconsistently applied. Nevertheless, case law suggests a need to broaden the scope of evidence beyond that of professional custom to establish medical malpractice. Part II, our case studies, show that pharmaceutical companies, through various pathways of influence, disrupt the legal standard of professional custom. Corporate influence over prescribing through impact on government regulation, medical education, scientific studies, and markets creates a false sense of professional custom. When these customs are used to determine tort liability, they undermine the form and function of the law and eliminate the protection of last resort for patients—private litigation for patient harms. These influences also disrupt the practice of medicine, creating a difficult situation for physicians when common practice does not align with the best interests of their patients. Part III further distills our doctrinal proposal within the practice of law and medicine and reconciles it with the history of professional custom. It also addresses historical counterarguments about moving toward a reasonableness standard in medical malpractice.

While this Article is focused on the role of custom in prescribing and the corporate pathways of influence that affect it, our conclusions have important implications for medical malpractice generally and to the "learned professions" more broadly. Corporate influence is not limited to pharmaceuticals; it increasingly pervades every aspect of the health care landscape and beyond. Private equity firms

now own many hospitals[396] and physician practices,[397] and the practice of medicine in general is dominated by insurance companies' control over reimbursement for medical services. Similarly, corporations own some accounting and law firms.[398] The dangers of corporate ownership are not hypothetical; a recent survey showed 25 percent more hospital-acquired patient medical complications in private equity-owned hospitals.[399]

The view that professional judgment is independent and isolated is increasingly more of a myth than a reality, and relying on professional practice alone to establish the standard of care in tort is thereby problematic. This Article lays the groundwork for a departure from professional custom for determining breach in medical malpractice prescribing cases. Further exploration of the application of a reasonable person instead of a professional custom standard in medical malpractice writ large as well as for the other learned professions is warranted elsewhere. The preservation of tort law as a means of private regulation of the legally recognized professions is vital, as litigation often serves as the protection of last resort for patients and clients.

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396. Alan Condon, *386 Hospitals Now Owned by Private Equity Firms: 6 Things to Know*, BECKER'S HOSP. CFO REP. (Dec. 19, 2023), https://www.beckershospitalreview.com/finance/386-hospitals-now-owned-by-private-equity-firms-6-things-to-know.html [https://perma.cc/VM5F-Q7K8] ("The 386 private equity-owned hospitals represent 9% of all private hospitals and 30% of all proprietary for-profit hospitals.... More than 24% ... are psychiatric hospitals.").

397. David Blumenthal, *Private Equity's Role in Health Care*, COMMONWEALTH FUND (Nov. 17, 2023), https://www.commonwealthfund.org/publications/explainer/2023/nov/private-equity-role-health-care [https://perma.cc/EJ9U-DH9T] ("[I]n 13 percent of metropolitan areas, a single private equity firm owns more than half of the physician market for certain specialties.").

398. Sam Skolnik & Kelcee Griffis, *Investment Bank-Backed Patent Shop Adds 'Law Firm' to Its Resumé*, BLOOMBERG LAW (Mar. 1, 2023, 5:09 AM), https://www.bloomberglaw.com/bloomberglawnews/business-and-practice/X6QGMC20000000?bna_news_filter=business-and-practice#jcite [https://perma.cc/3HG8-HXAU].

399. Brenda Goodman, *Private Equity Ownership of Hospitals Made Care Riskier for Patients, a New Study Finds*, CNN (Dec. 27, 2023, 11:12 AM), https://www.cnn.com/2023/12/26/health/private-equity-hospitals-riskier-health-care/index.html [https://perma.cc/U8RH-QHGC].