OFF-LABEL PREEMPTION

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A significant body of scholarship examines when federal law regulating drugs and devices preempts state law claims against manufacturers for defective products based on uses approved by the Food and Drug Administration (FDA)—what are called on-label uses. Yet scholars have paid little attention to how preemption applies to claims against manufacturers that promote uses FDA has not approved—what are called off-label uses. The omission is significant. Off-label use is widespread (comprising a significant portion of all uses) and risky (frequently unsupported by scientific evidence). In private lawsuits against manufacturers that promote off-label uses, preemption is often the linchpin issue. Courts analyzing whether federal law preempts state law claims based on off-label promotion have reached wildly inconsistent results. Despite the issue's importance, few scholars have systematically evaluated the off-label preemption landscape or provided a coherent rationale for how courts should apply preemption doctrine to state law claims based on off-label promotion.

This Article does both by developing an *approval theory* of off-label preemption that anchors doctrinal analysis to FDA's central function: ex ante risk evaluation of *approved uses* of drugs and devices. Emphasizing FDA ex ante review of use-based risks delivers three significant payoffs. First, it provides an organizing principle that explains the Supreme Court's seemingly fractured preemption jurisprudence. Second, the theory unifies conflicting approaches to preemption of state law claims based on off-label promotion. Finally, it offers a normative reason for why preemption should not apply to most state law claims based on off-label promotion of any drug or device.

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INTRODUCTION

In 2002, the Food and Drug Administration (FDA) approved a new medical device, InFuse Bone Graft, for use in operations to fuse the lumbar spine of adults with deteriorating vertebral cartilage.[1] Soon after approval, however, physicians began using the device in ways FDA had not approved—what are called off-label uses—including fusion of the upper spine.[2] Off-label use was so pervasive, in fact, that it was alleged to have accounted for nearly eighty-five percent of all InFuse sales.[3] One reason off-label use was so widespread was that the device's

1. Letter from Daniel Schultz, Deputy Dir. for Clinical & Rev. Pol'y, Off. of Device Evaluation Ctr. for Devices & Radiological Health, to Richard W. Treharne, Senior Vice President, Regul. Affs., Medtronic Sofamor Danek (July 2, 2002), https://www.accessdata.fda.gov/cdrh_docs/pdf/P000058A.pdf [hereinafter InFuse Bone Graft Approval Letter] (approving Premarket Approval Application no. P000058).

2. Nancy E. Epstein & Garry S. Schwall, *Costs and Frequency of "Off-Label" Use of INFUSE for Spinal Fusions at One Institution in 2010*, SURGICAL NEUROLOGY INT'L, Aug. 17, 2011, at 1.

3. Class Action Consolidated Complaint for Violation of the Federal Securities Laws at 3, *Minneapolis Firefighters' Relief Assoc. v. Medtronic, Inc.*, No. 08-cv-06324 (D. Minn. Aug. 21, 2009), 2009 WL 5185647.

manufacturer, Medtronic, promoted it.[4] After numerous reports of serious complications, patients started suing Medtronic for injuries they attributed to the device's off-label use.[5] At least one or more of their claims alleged that Medtronic should be liable for off-label promotion under state law for their injuries.[6] Similar stories pervade the drug context.[7]

Courts confronted with claims like these—state law liability claims based on off-label promotion—have reached inconsistent conclusions about their viability. Despite the ability to plead at least twelve different theories of liability under state law,[8] the legal survival of every theory turns on whether and when federal drug and device law preempts, or displaces, state law. Because the preemption analysis may turn on the specific theories of liability, courts often evaluate the issue on a claim-by-claim basis.[9]

Perhaps inevitably, the result has been doctrinal complexity and inter-circuit conflict.[10] Statutory language is at least partially to blame. Devices are subject to a preemption provision in federal law while prescription drugs are not.[11] Other aspects of this complexity, however, are related to the doctrine of preemption more broadly. Courts, for instance, have developed conflicting views about when preemption

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4. At least, it was alleged to have done so. Complaint for Damages at 39–43, *Ramirez v. Medtronic, Inc.*, 961 F. Supp. 2d 977 (D. Ariz.), *clarified on denial of reconsideration* (Oct. 24, 2013) (No. 13-cv-00512), 2013 WL 1089587.

5. *See, e.g.*, *Houston v. Medtronic, Inc.*, 957 F. Supp. 2d 1166 (C.D. Cal. 2013); *Beavers-Gabriel v. Medtronic, Inc.*, 15 F. Supp. 3d 1021 (D. Haw. 2014); Complaint for Damages, *supra* note 4.

6. Complaint for Damages, *supra* note 4, at 34.

7. The most well-known case involves Neurontin, which generated a broad range of civil and criminal litigation. *See, e.g.*, *In re Neurontin Mktg. & Sales Pracs. Litig.*, 342 F. Supp. 2d 1350 (J.P.M.L. 2004); Press Release, U.S. Dep't of Just., Warner-Lambert To Pay $430 Million To Resolve Criminal & Civil Health Care Liability Relating to Off-Label Promotion (May 13, 2004), https://www.justice.gov/archive/opa/pr/2004/May/04_civ_322.htm [https://perma.cc/RF8U-RD3M]. But there are others. *See, e.g.*, *Proctor v. Davis*, 682 N.E.2d 1203, 1215 (Ill. App. Ct. 1997).

8. This Article groups these theories into three doctrinal categories, but there are multiple claims under each theory. *See infra* Section I.B. For an example of a plaintiff alleging twelve claims, see *Jenkins v. Medtronic, Inc.*, 984 F. Supp. 2d 873, 876 (W.D. Tenn. 2013).

9. *See, e.g.*, *Bass v. Stryker Corp.*, 669 F.3d 501, 514–16 (5th Cir. 2012); *Schouest v. Medtronic, Inc.*, 13 F. Supp. 3d 692, 705–08 (S.D. Tex. 2014); *Hafer v. Medtronic, Inc.*, 99 F. Supp. 3d 844, 859–64 (W.D. Tenn. 2015). *See also infra* Part II.

10. *See, e.g.*, *Schouest*, 13 F. Supp. 3d at 700–02. Doubtless this is true for preemption of on-label claims against manufacturers as well. *See infra* Section II.B.

11. *See* Leanne Hay, Comment, *Stopping the Confusion: Why Widening the Preemption Gap Through the Parallel-Claims Exception Promotes Off-Label Uses of Medical Devices*, 60 JURIMETRICS 83, 97–99 (2019).

applies, both as a general matter and as to specific claims.[12] All this confusion has a significant cost for the regulatory system, manufacturers, and patients who are injured by off-label uses.

Despite its importance, scholars have largely overlooked this problem,[13] focusing instead on preemption of state law claims that do not involve off-label promotion.[14] This focus is understandable. Although claims against manufacturers have generated a number of important Supreme Court preemption cases in the past thirty years, none involved off-label promotion.[15] These claims are also broadly applicable to state

12. *See Schouest*, 13 F. Supp. 3d at 701–03.

13. *But see, e.g.*, Leanne Hay, *supra* note 11, at 96–101 (arguing that parallel claims exception to express preemption should be expanded to cover off-label promotion).

14. *See, e.g.*, Patricia J. Zettler, Annamarie Beckmeyer, Beatrice L. Brown & Ameet Sarpatwari, *Mifepristone, Preemption, and Public Health Federalism*, J. L. & BIOSCIENCES, July–Dec. 2022, at 1; Patricia J. Zettler & Ameet Sarpatwari, *State Restrictions on Mifepristone Access — the Case for Federal Preemption*, 386 N. ENG. J. MED. 705 (2022); George Horvath, *Emergent Regulatory Systems and Their Challenges: The Case of Combination Medical Products*, 94 WASH. L. REV. 1697, 1738–53 (2019) (discussing combination products); Aaron D. Twerski, Essay, *The Demise of Drug Design Litigation: Death by Federal Preemption*, 68 AM. U. L. REV. 281 (2018); Elizabeth Y. McCuskey, *On Drugs: Preemption, Presumption, and Remedy*, 38 J. LEGAL MED. 365 (2018); Max N. Helveston, *Preemption Without Borders: The Modern Conflation of Tort and Contract Liabilities*, 48 GA. L. REV. 1085 (2014); Lisa M. Mottes, Comment, *The Need for Federal Preemption of State Tort Claims in the Context of "New Drugs" and Premarket-Approved Medical Devices*, 41 SETON HALL L. REV. 723 (2011); Amanda N. Hart, Note, *Federal Preemption of State-Law Failure-To-Warn Claims: Has the Presumption Against Preemption Gone Too Far?*, 6 SEVENTH CIR. REV. 308 (2010); Elizabeth J. Cabraser, *Due Process Preempted: Stealth Preemption as a Consequence of Agency Capture*, 65 N.Y.U. ANN. SURV. AM. L. 449 (2010); Jodie M. Gross & Judi Abbott Curry, *The Federal Preemption Debate in Pharmaceutical Labeling Product Liability Actions*, 43 TORT TRIAL & INS. PRAC. L.J. 35 (2007); David C. Vladeck, *Preemption and Regulatory Failure*, 33 PEPP. L. REV. 95 (2005); Catherine M. Sharkey, *Products Liability Preemption: An Institutional Approach*, 76 GEO. WASH. L. REV. 449 (2008) [hereinafter *Products Liability Preemption*]; Richard A. Epstein, *The Case for Field Preemption of State Laws in Drug Cases*, 103 NW. U. L. REV. COLLOQUY 54 (2008), https://scholarlycommons.law.northwestern.edu/cgi/viewcontent.cgi?article=1129&context=nulr_online; Christine H. Kim, *The Case for Preemption of Prescription Drug Failure-To-Warn Claims*, 62 FOOD & DRUG L.J. 399 (2007); Jonathan V. O'Steen & Van O'Steen, *The FDA Defense: Vioxx® and the Argument Against Federal Preemption of State Claims for Injuries Resulting from Defective Drugs*, 48 ARIZ. L. REV. 67 (2006); Bruce Patsner, Riegel v. Medtronic, Inc.*: Revisiting Pre-Emption for Medical Devices*, 37 J. L. MED. & ETHICS 305 (2009); Catherine M. Sharkey, *What* Riegel *Portends for FDA Preemption of State Law Products Liability Claims*, 102 NW. U. L. REV. COLLOQUY 415 (2008), https://scholarlycommons.law.northwestern.edu/cgi/viewcontent.cgi?article=1123&context=nulr_online [hereinafter *What* Riegel *Portends*]; David C. Vladeck, *FDA Preemption,* Wyeth*, Congress, and a Crystal Ball*, 32 HAMLINE L. REV. 707 (2009).

15. *Medtronic, Inc. v. Lohr*, 518 U.S. 470 (1996); *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341 (2001); *Riegel v. Medtronic, Inc.*, 552 U.S. 312 (2008); *Wyeth v. Levine*, 555 U.S. 555 (2009); *PLIVA, Inc. v. Mensing*, 564 U.S. 604 (2011);

law claims challenging the safety of drugs or devices, raising important questions about whether the manufacturer could or should have done something over and above, or different from, existing regulatory requirements.

Off-label promotion, however, is no less important. A large percentage of uses—in some practice areas up to eighty percent—occur off-label.[16] While many of these uses are innovative or medically necessary, they also present unique risks that FDA has not reviewed and with which physicians are unfamiliar.[17] Exacerbating the concern over the risk of off-label use is the well-documented financial incentive manufacturers have to promote off-label uses to increase sales.[18]

Because off-label use is both risky for patients and profitable for manufacturers, many scholars and policymakers have proposed ideas to rein in the practice when it is unsupported by evidence, with some focusing specifically on promotion.[19] And while state tort claims are a

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Mut. Pharm. Co. v. Bartlett, 570 U.S. 472 (2013); *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668 (2019).

16. David C. Radley, Stan N. Finkelstein & Randall S. Stafford, *Off-Label Prescribing Among Office-Based Physicians*, 166 ARCHIVES INTERNAL MED. 1021, 1023 (2006); S. Balan, M. A. Hassali & V. S. L. Mak, *Awareness, Knowledge and Views of Off-Label Prescribing in Children: A Systematic Review*, 80 BRITISH J. CLINICAL PHARMACOLOGY 1269, 1269 (2015).

17. *See, e.g.*, Donna T. Chen, Matthew K. Wynia, Rachael M. Moloney & G. Caleb Alexander, *U.S. Physician Knowledge of the FDA-Approved Indications and Evidence Base for Commonly Prescribed Drugs: Results of a National Survey*, 18 PHARMACOEPIDEMIOLOGY & DRUG SAFETY 1094 (2009); Walter Smalley, Deborah Shatin, Diane K. Wysowski, Jerry Gurwitz, Susan E. Andrade et al., *Contraindicated Use of Cisapride: Impact of Food and Drug Administration Regulatory Action*, 284 JAMA 3036 (2000). Physicians may be more reactive to FDA action. *See, e.g.*, Supriya K. Bhatia, Amy J. Rezac-Elgohary, Benedetto Vitiello, Michael S. Sitorius & Bruce A. Buehler, *Antidepressant Prescribing Practices for the Treatment of Children and Adolescents*, 18 J. CHILD & ADOLESCENT PSYCHOPHARMACOLOGY 70 (2008).

18. Much of the documentation comes from lawsuits brought by whistleblowers or the federal government, and sometimes private payors. For one prominent example, see Tracy Staton, *Pfizer Adds Another $325M to Neurontin Settlement Tally. Total? $945M*, FIERCE PHARMA (June 2, 2014, 4:40 PM), https://www.fiercepharma.com/sales-and-marketing/pfizer-adds-another-325m-to-neurontin-settlement-tally-total-945m [https://perma.cc/Y4NH-GHHE]; Jeanne Lenzer, *Pfizer Pleads Guilty, but Drug Sales Continue To Soar*, 328 BMJ 1217 (2004). Sometimes information comes from securities lawsuits. *See, e.g.*, Second Amended Complaint at 54–63, *Ferraro Fam. Found., Inc. v. Corcept Therapeutics Inc.*, 501 F. Supp. 3d 735 (N.D. Cal. 2020) (No. 19-cv-01372), 2020 WL 3958975.

19. *See, e.g.*, David A. Simon, *Off-Label Speech*, 72 EMORY L.J. 549 (2023); George Horvath, *Off-Label Drug Risks: Toward a New FDA Regulatory Approach*, ANNALS HEALTH L. & LIFE SCI., Winter 2020, at 101, 119–26; Cynthia M. Ho, *A Dangerous Concoction: Pharmaceutical Marketing, Cognitive Biases, and First Amendment Overprotection*, 94 IND. L.J. 773 (2019); Christopher Robertson, *When Truth Cannot Be Presumed: The Regulation of Drug Promotion Under an Expanding First*

natural place to look for regulatory support,[20] few scholars have systematically explained the off-label preemption landscape or provided a coherent rationale for how courts should apply preemption doctrine to state law claims based on off-label promotion.[21]

This Article does both by developing a theory of off-label preemption that anchors doctrinal analysis to FDA's central function: ex ante risk evaluation of *particular uses* of drugs and devices. It contends that the fractured preemption jurisprudence results from a misunderstanding of the doctrine and purpose of both FDA regulation and preemption. Drawing on the work of Catherine Sharkey, it proposes a remedy by developing an *approval-based* theory of off-label preemption where FDA's approval of *particular uses* determines whether state law claims about particular use-based risk are preempted.[22] Under this theory, the central question is whether FDA review identifies risks *related to the use* that harms the patient *and* provides notice that it has reviewed for that risk. Because off-label promotion often concerns uses and (some) attendant risks FDA has not yet evaluated or evaluated in the

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Amendment, 94 B.U. L. REV. 545 (2014); Stephanie M. Greene, *After* Caronia*: First Amendment Concerns in Off-Label Promotion*, 51 SAN DIEGO L. REV. 645 (2014); Aaron S. Kesselheim & Michelle M. Mello, *Prospects for Regulation of Off-Label Drug Promotion in an Era of Expanding Commercial Speech Protection*, 92 N.C. L. REV. 1539 (2014); Fazal Khan & Justin Holloway, *Verify, Then Trust: How To Legalize Off-Label Drug Marketing*, 117 PA. ST. L. REV. 407, 408 (2012). The literature here is vast. For a more comprehensive list, see Simon, *supra*, at 551–56.

20. Other avenues exist for private enforcement, including securities law violations and civil RICO violations, though these have significant limitations. *See, e.g.*, *Ferraro Fam. Found., Inc.*, 501 F. Supp. 3d at 744 (securities fraud class action); *Painters & Allied Trades Dist. Council 82 Health Care Fund v. Takeda Pharms. Co.*, 943 F.3d 1243 (9th Cir. 2019) (claim alleging civil RICO violations).

21. For a comprehensive treatment of the totality of issues involving off-label use, including a discussion of preemption in this context, see James M. Beck, *Off-Label Use in the Twenty-First Century: Most Myths and Misconceptions Mitigated*, 54 UIC J. MARSHALL L. REV. 1 (2021). *See also* James M. Beck & Elizabeth D. Azari, *FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions*, 53 FOOD & DRUG L.J. 71 (1998). Beck gives the most in-depth treatment so far. Beck, *supra*, at 60–84. *See also* Marcia Boumil, *FDA Approval of Drugs and Devices: Preemption of State Laws for "Parallel" Tort Claims*, 18 J. HEALTH CARE L. & POL'Y 1, 41–43 (2015); Jeffrey Chasnow & Geoffrey Levitt, *Preemption of Non-Federal Restraints on Off-Label Product Communications*, 71 FOOD & DRUG L.J. 249, 264–70 (2016).

22. In part, this theory is an extension of Catherine Sharkey's "agency reference model," though it differs in an important respect. *Products Liability Preemption*, *supra* note 14, at 452–53. Under Sharkey's model, federal law preempts state law claims where FDA has "made a specific determination about a particular risk at the time the cause of action arises." *See id.* at 513. Under the approval theory, however, preemption does not apply even when FDA has made a specific determination about a particular on-label risk if the risk is not labeled or concerns a labeled risk that is not equally applicable to the promoted off-label use. *See infra* Section III.A. To the extent Sharkey's theory can be read this way, this Article adopts her theory.

same manner as on-label uses,[23] many risks never make it on the drug label or are otherwise communicated to physicians, so drug and device manufacturers that promote their devices off-label should be liable when that off-label promotion also violates duties imposed by contract, tort, and other state laws.

This last point is important. It means that FDA review of a particular off-label use, or risks associated with it, does not necessarily resolve the preemption question.[24] Even when FDA considers a use that it does not ultimately approve, its review may be limited: FDA may not fully consider all the risks associated with the use or opine on their significance. Indeed, it may mean precisely the opposite: there was not sufficient information to determine the relative risks associated with the use or the risks outweighed the benefits. And without FDA *approval*, an off-label use and at least some of the risks associated with it will not appear on the label.[25] Some on-label risks, of course, may apply to off-label uses—and some aspect of them may even appear on the labeling. And where the on-label risk applies equally to the off-label use, the problem posed by off-label promotion may not exist. In such cases, preemption *may* apply, but the plaintiff should be able to argue that the on-label risks are *not* equally applicable based on either scientific evidence or the manufacturer's promotional activity (or a combination of the two).[26]

For many tort and contract claims involving drugs and devices, the label is what provides notice sufficient to discharge a manufacturer's duty to warn of risks associated with the use. Physicians cannot know whether FDA reviewed an off-label use and the risks associated with it in some way, or to what degree, because those unapproved uses are not on the label. And without that information, physicians lack notice of the risks associated with the off-label use absent some affirmative action by the manufacturer. Because FDA's process has not provided notice of its review by approving the labeling of the use, manufacturers that promote off-label uses should therefore be responsible for providing the notice

23. FDA expressly considers some off-label uses that must appear on the label. *See infra* notes 204–07 and accompanying text.

24. This is an important distinction between the approval theory and Sharkey's agency-reference model. Preemption should not apply to a risk arising from off-label use that does not appear on the labeling *even if* FDA has made a "specific determination" as to that risk. Stated differently, the approval theory refines or clarifies Sharkey's approach by pointing out that risks are *use-based* determinations.

25. *See infra* Section I.A.

26. For a complete explanation, see *infra* Section III.A.

FDA has not or cannot.[27] When manufacturers fail to do so, preemption should not block state law claims based on a promoted off-label use.

In developing and arguing for the approval-based theory, this Article makes two contributions: One is descriptive. By explaining and plotting the existing preemption law on off-label uses, it provides a roadmap for legal decisionmaking in an area where courts have "struggle[d]" with "[e]ven the usually straightforward job of laying out the rules" relating to preemption.[28] This is "no easy task."[29] But it is essential to understanding when and why preemption applies to state law claims against drug and device manufacturers.

The second is normative. The approval theory offers a way to unite the disparate and conflicting preemption frameworks applicable to drugs and devices while preserving fidelity to Supreme Court precedent. Underlying the Court's jurisprudence, this Article argues, is a unifying *thoroughness principle*: preemption's scope is determined by whether and how thoroughly FDA has reviewed the risk that a claimant alleges has materialized and injured them.[30] When FDA engages in a thorough review—often one that results in a specific mandate—the Court has found preemption applies more broadly than when the FDA's review is less searching or nonexistent. This explains why preemption applies more expansively to drugs and certain devices that undergo the most stringent review for safety and efficacy than to devices that undergo a review for equivalence instead of safety and efficacy.

Besides explaining the existing Supreme Court preemption jurisprudence and showing why this theory is a logical extension of it, this analysis also unifies the doctrine it explains. By examining the case law to develop the theory and the principle underlying it, this Article demonstrates not only that the unification makes theoretical sense, but also that many doctrinal mistakes are responsible for its partition. These mistakes are significant. For example, the approval theory of preemption shows that federal law should not, contrary to many court decisions,

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27. If firms argue they are prohibited from providing this risk information because it violates federal law, then they should be prohibited from promoting the use for the same reason. *See infra* Section III.C.1. On the other hand, if firms can promote the use, then they are *obligated* to disclose risk information under state law. For a discussion of whether preemption applies to labeled risks that apply to off-label use, see *infra* Section III.A.

28. *Caplinger v. Medtronic, Inc.*, 784 F.3d 1335, 1340 (10th Cir. 2015) (quoting *Schouest v. Medtronic, Inc.*, 13 F. Supp. 3d 692, 700 (S.D. Tex. 2014)).

29. *Id.* (quoting *Martin v. Medtronic, Inc.*, 254 F.3d 573, 579 (5th Cir. 2001), discussing *Medtronic, Inc. v. Lohr*, 518 U.S. 470 (1996)).

30. Not all risks on the label are on-label risks. As discussed *infra* Section II.C.2, FDA requires manufacturers to include on the label risk information for particular about off-label uses for drugs.

preempt the design and warning defect claims against Medtronic based on its off-label promotion of the InFuse Bone Graft discussed before. Nor should it preclude state law claims against drug manufacturers based on off-label promotion, including at least some claims against manufacturers of generic drugs. By leaning on the thoroughness principle, the approval theory breaks away twisted and conflicting strands of jurisprudence that have emerged from courts' attempts to stitch together seemingly different doctrinal rules.

Ultimately, however, appeals to theoretical coherence or legal consistency are part of a larger policy-based justification of the theory: limiting *harmful* off-label promotion in a world where the practice is increasingly difficult to rein in. This Article argues that there are strong policy reasons—ranging from reducing information asymmetries to ensuring quality drug and device innovation—to adopt the approval theory of off-label preemption.[31]

The Article proceeds as follows. Part I explains drug and device approval, off-label use and promotion, and the state law theories that underpin most claims against drug and device manufacturers. Part II comprehensively lays out the preemption doctrine and explains how courts apply it to drugs and devices for both on-label uses and off-label promotion. Part III presents the case for an approval theory of preemption. It shows how the theory helps to identify and correct doctrinal mistakes that cleave judicial approaches to preemption. After explaining how the approval theory facilitates and supports doctrinal corrections, it offers five policy reasons that provide additional support for the theory.

I. OFF-LABEL USE, PROMOTION, AND PRIVATE LAW CLAIMS

This Part explains off-label use, promotion, and theories of liability applicable to them. Section I.A briefly describes the regulatory review process for drugs and devices. It then explains off-label use, highlighting both the necessity of the practice and the tradeoffs inherent in promoting it. Section I.B describes the suite of claims typically alleged in lawsuits against drug and device manufacturers stemming from off-label promotion.

31. *See infra* Section III.C. This does not mean to suggest that law and policy are divorced. It means only that some rules are internal to legal doctrine and appeal to its logic, while others explicitly identify an objective that grafts onto those rules or provides other reasons to accept or change them.

A. Drugs and Devices, Off-Label Use, and Promotion

Drugs and devices can reach the market only by passing through different pathways mandated by the Food, Drug, and Cosmetic Act (FDCA).[32] Drugs typically undergo a long and time-consuming review only after completing several phases of clinical trials, often at a cost exceeding $1 billion.[33] High risk devices undergo a similar process to obtain premarket approval (PMA) from FDA, though with less expense (around $500 million) and with fewer and different types of clinical trials.[34] Most devices, however, are intermediate risk and reach the market when the FDA "clears" them after review under the less-demanding 510(k) process.[35] Unlike the PMA process, the 510(k) process does not typically require pivotal clinical trials.[36] Instead, manufacturers can obtain clearance by demonstrating that their device is substantially equivalent to a legally marketed device.[37]

Approval or clearance, however, is not a license to sell or market the product for any and all uses the manufacturer wants. It is permission

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32. Pub. L. No. 75-717, 52 Stat. 1040 (codified as amended in scattered sections of 21 U.S.C.). There are a variety of nuances and pathways available to both drugs and devices. *See Development & Approval Process | Drugs*, FDA, https://www.fda.gov/drugs/development-approval-process-drugs (Aug. 8, 2022); *How To Study and Market Your Device*, FDA, https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/how-study-and-market-your-device (Oct. 12, 2023). For simplicity, this Article focuses on the "standard" pathways.

33. Joseph A. DiMasi, Henry G. Grabowski & Ronald W. Hansen, *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. HEALTH ECON. 20, 31–32 (2016); Joseph A. DiMasi, Ronald W. Hansen & Henry G. Grabowski, *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151 (2003).

34. Aylin Sertkaya, Rebecca DeVries, Amber Jessup & Trinidad Beleche, *Estimated Cost of Developing a Therapeutic Complex Medical Device in the US*, JAMA NETWORK OPEN, Sept. 2022, at 1, 5–6 (2022); Jonathan J. Darrow, Jerry Avorn & Aaron S. Kesselheim, *FDA Regulation and Approval of Medical Devices: 1976-2020*, 326 JAMA 420, 426 (2021).

35. COMM. ON THE PUB. HEALTH EFFECTIVENESS OF THE FDA 510(k) CLEARANCE PROCESS, INST. OF MED. OF THE NAT'L ACADS., MEDICAL DEVICES AND THE PUBLIC'S HEALTH: THE FDA 510(k) CLEARANCE PROCESS AT 35 YEARS 4, 170 (2011).

36. *See* Darrow, Avorn & Kesselheim, *supra* note 34, at 421.

37. 21 U.S.C. §§ 360(k), 360c(f)(1), (i). This is called a "predicate device" and includes devices that are no longer on the market, including those recalled for safety risks. The predicate device and the new device must have the same intended use, among other things. *See* 21 U.S.C. § 360c(i); 21 C.F.R. § 807.92(a)(3) (2024); CTR. FOR DEVICES & RADIOLOGICAL HEALTH & CTR. FOR BIOLOGICS EVAL. & RSCH., FDA, THE 510(k) PROGRAM: EVALUATING SUBSTANTIAL EQUIVALENCE IN PREMARKET NOTIFICATIONS [510(k)]: GUIDANCE FOR INDUSTRY AND FOOD AND DRUG ADMINISTRATION STAFF 10–11 (2014) [hereinafter 510(k) GUIDANCE].

for the manufacturer to sell or market the product for its "intended use"—the conditions under which FDA has reviewed (*i.e.*, indication, dosage, patient population). Approval or clearance *requires* the manufacturer label the drug or device in a specific manner that describes these intended uses, along with their potential risks and benefits.[38]

For healthcare practitioners,[39] however, the label is less constraining. They may often prescribe, administer, or use the drug or device in a manner that does not appear on or is inconsistent with the labeling.[40] This practice is known as "off-label" use because the use to which the drug or device is put does not appear on the labeling—it is not the intended use.[41]

FDA's decision to grant marketing authorization for a drug or device is focused on and relative to on-label uses, rather than potential off-label ones. In other words, FDA does not review drug or device

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38. 21 U.S.C. §§ 352(f), 355, 360c, 360e. *See also* 21 C.F.R. pt. 201 (drug labeling); 21 C.F.R. § 201.100(d)(1) (requiring "adequate information" for use for prescription drugs to avoid misbranding violations under Section 352).

39. In the United States, the term includes prescribing by non-physicians, such as nurse practitioners and physicians' assistants. *See, e.g.*, *Levine v. Am. Home Prods., Inc.*, No. 670-12-01, at 1 (Vt. Super. Ct. July 30, 2004), 2004 WL 5456809, at *1 (noting physician assistant administered medication). Additionally, for physicians who work in hospitals or large medical systems, the ultimate decisionmaking authority may reside with other parts of the larger organization, such as the pharmacy and therapeutics committee. *See* David A. Simon, *Off-Label Innovation*, 56 GA. L. REV. 701, 740–49 (2022).

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

41. Physicians are not completely unconstrained. Federal and state laws, for example, can prohibit certain types of off-label prescribing. *See, e.g.*, 21 U.S.C. § 333(e)(1) (prohibiting physicians from "knowingly distribut[ing], or posses[ing] with intent to distribute, human growth hormone for any use other than the treatment of a disease or other recognized medical condition"). Indeed, compared to federal laws that have significant bite—like the False Claims Act, 31 U.S.C. §§ 3729–33, the Antikickback Statute, 42 U.S.C. § 1320a–7b(b), and the Stark Law, 42 U.S.C. § 1395nn(g)—tort liability seems decidedly slack jawed. *See also* David A. Simon, Gatekeepers of Medical Innovation 14 (unpublished manuscript) (on file with author) (describing how Medicare reimbursement can limit off-label prescribing). But tort liability for *physicians* prescribing off-label is rare: A search of Westlaw and Lexis returns less than forty published cases. In fact, state law may *limit* liability of physicians and insurance companies who prescribe drugs for certain off-label uses. *See, e.g.*, MASS. GEN. LAWS ch. 176G, § 4E (2023). *See also* KAN. LEGIS. RSCH. DEP'T, SUPPLEMENTAL NOTE ON HOUSE BILL NO. 2280: AS AMENDED BY SENATE COMMITTEE ON PUBLIC HEALTH AND WELFARE 2, https://www.kslegislature.org/li_2022/b2021_22/measures/documents/supp_note_hb2280_04_0000.pdf [https://perma.cc/RVZ4-T9VB] (describing the bill's proposal to limit liability for off-label prescriptions with patient waivers).

applications to evaluate or validate all potential off-label uses.[42] Instead, it devotes its attention to the narrow and particularized question of whether the drug or device is safe and effective under the applied for conditions of use.[43]

That does not mean, however, that FDA never considers any off-label risks when reviewing drug or device applications. Sometimes the manufacturer applies for labeling that includes uses that FDA rejects (making them off-label uses); other times labeling regulations require the manufacturer to include information in its application information about certain potentially high-risk off-label uses.[44] FDA can also consider the safety risks of the drug and impose conditions on dispensing and use that minimize them.[45] Once a drug or device is on the market, FDA has the authority to require that manufacturers provide warnings to physicians and healthcare providers through labeling changes and letters,[46] perform additional studies,[47] and remove or recall it from the market.[48] In exercising these powers, FDA may consider some off-label uses of a drug, though nothing requires it to do so. Thus, while FDA does not expressly consider all potential off-label uses when making an approval

42. Some scholars argue that FDA should go further, using its authority to consider information beyond the intended use, specifically public health consequences, in approving drugs. *See* Patricia J. Zettler, Margaret Foster Riley & Aaron S. Kesselheim, *Implementing a Public Health Perspective in FDA Drug Regulation*, 73 FOOD & DRUG L.J. 221 (2018); Patricia J. Zettler, *The Indirect Consequences of Expanded Off-Label Promotion*, 78 OHIO ST. L.J. 1053, 1087–90 (2017).

43. *See Understanding Unapproved Use of Approved Drugs "Off Label," supra* note 40. The term "safe and effective" here is meant to encompass all of the potential types of review, each of which may embody some concept of "safety and effectiveness" even if the precise standard is different. *See, e.g.*, 510(k) GUIDANCE, *supra* note 37, at 6–7 (noting that "[s]afety and effectiveness" is factored into both the "substantial equivalence" standard under Section 510(k) and the "reasonable assurance of safety and effectiveness" standard for PMA).

44. *See infra* Section II.C.

45. 21 U.S.C. §§ 355–1, 355(o).

46. 21 C.F.R. § 200.5 (2024). *See also* CTR. FOR DRUG EVALUATION & RSCH. & CTR. FOR BIOLOGICS EVALUATION & RSCH., FDA, OMB CONTROL NO. 0910-0754, GUIDANCE FOR INDUSTRY AND FDA STAFF: DEAR HEALTH CARE PROVIDER LETTERS: IMPROVING COMMUNICATION OF IMPORTANT SAFETY INFORMATION 4 (2014), https://www.fda.gov/media/79793/download.

47. 42 U.S.C. § 262; 21 U.S.C. § 355(o)(3)(C).

48. *E.g.*, 42 U.S.C. § 262(d)(1) (recall of biologics); 21 U.S.C. § 355(e) (withdrawal of drug approval); 21 U.S.C. § 356(c)(3) (expedited withdrawal of accelerated approval); 21 C.F.R. §§ 314.150–53 (withdrawal of approval of new drug or abbreviated new drug application); 21 C.F.R. §§ 7.40–.42, 7.45 (recall procedures); 21 U.S.C. § 360h(a) (device-related notifications); 21 U.S.C. § 360h(e) (device recall authority); 21 C.F.R. pt. 810 (recall of devices); 21 U.S.C. § 360e(e) (withdrawal and temporary suspension of PMA); 21 C.F.R. § 814.46–.47 (withdrawal and temporary suspension of PMA approval).

decision, it may evaluate some off-label risks before or after marketing approval.[49] In general, however, evaluation of off-label risks is not the primary focus or function of FDA approval decisions—nor of its post-market authorities that bear on drug use.[50]

Although FDA does not review all off-label risks, off-label use nevertheless occurs for a variety of reasons. Legally, FDA claims it does not regulate the practice of medicine, though it may regulate various aspects of both off-label prescribing and the practice of medicine in other ways.[51] Practically, prescribing off-label may be the standard of care or otherwise in the best interests of the patient, who may lack any on-label treatment. This is important for a variety of practice areas, particularly pediatrics, geriatrics, and oncology.[52] Off-label use is also a source of innovation, with physicians using their training and experience to find new uses for old drugs.[53] But off-label uses are potentially riskier than on-label ones because they generally have not undergone FDA review. Evidence supporting them is, consequently, typically lower in quantity and quality than evidence supporting on-label uses.

Despite the potential drawbacks, off-label use can be quite profitable for drug companies that hold patents or regulatory exclusivities, which they can use to prevent competition.[54] By and large, each additional sale

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49. It is also important to separate off-label uses generally with off-label uses contraindicated by the labeling. The latter FDA has considered; the former it generally has not. Claims against manufacturers that (unwisely) promote uses FDA has found expressly contraindicated should escape preemption but not under the approval theory. Here a straight parallel claims analysis—one based on false or misleading statements—works fine.

50. *But see* Simon, *supra* note 19, at 558–77 (describing how FDA enforces the FDCA when off-label speech is involved).

51. For an argument that FDA regulates the practice of medicine, see Patricia J. Zettler, *Pharmaceutical Federalism*, 92 IND. L.J. 845 (2017); Patricia J. Zettler, *Toward Coherent Federal Oversight of Medicine*, 52 SAN DIEGO L. REV. 427, 454–77 (2015). For an argument that FDA should not regulate the practice of medicine and its regulation contributed to the blurred line between product and practice, see Myrisha S. Lewis, *Innovating Federalism in the Life Sciences*, 92 TEMP. L. REV. 383 (2019).

52. *See, e.g.*, Kathleen A. Neville, Daniel A.C. Frattarelli, Jeffrey L. Galinkin, Thomas P. Green, Timothy D. Johnson et al., Policy Statement, *Off-Label Use of Drugs in Children*, 133 PEDIATRICS 563 (2014); Stephen H.D. Jackson, Paul A.F. Jansen & Arduino A. Mangon, *Off-Label Prescribing in Older Patients*, DRUGS & AGING, June 2012, at 427 (geriatrics); *Off-Label Drug Use*, AM. CANCER SOC'Y, https://www.cancer.org/cancer/managing-cancer/treatment-types/off-label-drug-use.html [https://perma.cc/3S9D-ATXP] (Mar. 17, 2015) (oncology).

53. *See, e.g.*, Simon, *supra* note 39 (studying CMS reimbursement for off-label uses as incentivizing innovation).

54. The scholarship on this topic is extensive. For some examples, see Robin Feldman, *May Your Drug Price Be Evergreen*, 5 J. L. & BIOSCIENCES 590 (2018); C. Scott Hemphill & Bhaven N. Sampat, *Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals*, 31 J. HEALTH ECON. 327 (2012); Michael S. Sinha,

of a drug for an off-label use counts the same as an on-label use. Manufacturers therefore have an incentive to increase off-label uses. One study in 2008, for example, estimated that $6 billion (around $8.6 billion in 2024 dollars) was spent on off-label use of antipsychotic medications alone.[55]

Because of its profitability, manufacturers may try to increase off-label uses (and sales) by promoting them to physicians using a variety of different mechanisms.[56] For example, they may send salespersons to "detail" physicians and extoll them on the virtues of the new drug or device.[57] Or, they may fly them to desirable locations for conferences to learn about the product.[58]

While increasing information about off-label uses to physicians has some benefits, it also can cause physicians to use drugs and devices in unsafe ways. Depending on how it is done, off-label promotion can leave out important details or fail to disclose certain risk information that

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Public Health Product Hops, 73 AM. U. L. REV. 395 (2023); Dmitry Karshtedt, *The More Things Change: Improvement Patents, Drug Modifications, and the FDA*, 104 IOWA L. REV. 1129 (2019); Carolyne Hathaway, John Manthei & Cassie Scherer, *Exclusivity Strategies in the United States and European Union*, UPDATE, May/June 2009, at 34. Vandana Prajapati, Swagat Tripathy & Harish Dureja, *Product Lifecycle Management Through Patents and Regulatory Strategies*, 13 J. MED. MKTG. 171 (2013).

55. G. C. Alexander, S. A. Gallagher, A. Mascola, R. M. Moloney & R. S. Stafford, *Increasing Off-Label Use of Antipsychotic Medications in the United States, 1995–2008*, 20 PHARMACOEPIDEMIOLOGY & DRUG SAFETY 177, 181 (2011).

56. *E.g.*, Aaron S. Kesselheim, Michelle M. Mello & David M. Studdert, *Strategies and Practices in Off-Label Marketing of Pharmaceuticals: A Retrospective Analysis of Whistleblower Complaints*, PLOS MED., Apr. 2011, at 1, 5. Strategies for devices are similar, though not always identical. For example, device manufacturers often have sales reps in the operating room with physicians, a situation that can lead to off-label use. One recent study argues the effects of detailing on off-label use are small and can be counterproductive (resulting in legal costs that exceed revenues). Bradley T. Shapiro, *Informational Shocks, Off-Label Prescribing, and the Effects of Physician Detailing*, 64 MGMT. SCI. 5925, 5943–44 (2018). Effects of restrictions on off-label promotion are mixed, suggesting they lead to less brand–drug use overall but not necessarily less off-label use. *See* Ian Larkin, Desmond Ang, Jerry Avorn & Aaron S. Kesselheim, *Restrictions on Pharmaceutical Detailing Reduced Off- Label Prescribing of Antidepressants and Antipsychotics in Children*, 33 HEALTH AFFS. 1014, 1020–21 (2014). *See also Sorrell v. IMS Health Inc.*, 564 U.S. 552, 557–61 (2011).

57. On profitability of this practice, see Sridhar Narayanan, Ramarao Desiraju & Pradeep K. Chintagunta, *Return on Investment Implications for Pharmaceutical Promotional Expenditures: The Role of Marketing-Mix Interactions*, J. MKTG., Oct. 2004, at 90.

58. *See* Michael Totty, *Public Disclosure of Drug Company Gifts: High-Prescribing Physicians Unaffected*, UCLA ANDERSON REV. (Aug. 31, 2022), https://anderson-review.ucla.edu/public-disclosure-of-drug-company-gifts-high-prescribing-physicians-unaffected/ [https://perma.cc/6R7P-7HWK].

influences physician decisionmaking.[59] For example, one patient's estate alleged that the manufacturer of Botox, frequently used to treat muscle spasms, failed to warn her physician of a potential immune reaction that killed her.[60] Not all cases are so extreme, with unexpected "adverse events" from off-label use ranging from minor (*e.g.*, nausea) to moderate (*e.g.*, further treatment required) to severe *(e.g.*, hospitalization, disability, death).[61]

Practically, FDA's general position on off-label promotion is that it is harmful to patients and corrosive to the incentives that make the drug and device regulatory system tick.[62] Legally, FDA argues that off-label promotion is evidence of an FDCA violation.[63] Because the intended use of a drug or device is determined by the manufacturer's "objective intent,"[64] what the manufacturer says about its drug can change the drug's intended use. A manufacturer violates federal labeling law by introducing into commerce a drug with an intended use FDA has not approved. An example is advertising a drug to treat glaucoma even though FDA approved it to treat only gout.[65]

FDA takes the position that this kind of analysis extends to promotional activities like the ones described above. In particular, FDA has argued that off-label promotion violates federal law in three ways. First, off-label promotion introduces a new drug or device without proper approval or clearance.[66] Second, off-label promotion constitutes "misbranding" under the FDCA because it is "false or misleading in any

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59. Many off-label promotion theories focus on fraud and misrepresentation. While those claims should move forward, they should not serve as *limitations* on claims. Therefore, I deliberately avoid saying that the off-label promotion must *mislead* the physician. *See infra* Conclusion.

60. *Rosenstern v. Allergan, Inc.*, 987 F. Supp. 2d 795, 799–800 (N.D. Ill. 2013).

61. *See* Tewodros Eguale, David L. Buckeridge, Aman Verma, Nancy E. Winslade, Andrea Benedetti et al., *Association of Off-Label Drug Use and Adverse Drug Events in an Adult Population*, 176 JAMA INTERNAL MED. 55 (2016) (Canadian study).

62. Simon, *supra* note 19, at 551–52. Firms that can promote uses off-label have less incentive to generate data and submit the off-label uses to FDA than do firms that cannot promote off-label uses. *See* Rebecca S. Eisenberg, *The Problem of New Uses*, 5 YALE J. HEALTH POL'Y L. & ETHICS 717, 730–35 (2005).

63. Simon, *supra* note 19, at 552–53. Of course, it did not start from this position but retreated to it. *See id.* at 559–74.

64. 21 C.F.R. § 201.128 (2023).

65. 21 U.S.C. §§ 331, 333(a)–(b).

66. 21 U.S.C. § 321(p) (defining "new drug"); 21 U.S.C. § 355 (prohibiting introduction of new drugs); 21 C.F.R. § 201.128 (2024) (defining "intended uses" of drugs); 21 U.S.C. § 321(h) (defining "device"); 21 C.F.R. § 801.4 (defining "intended uses" of devices); 21 C.F.R. § 814.80 (prohibiting labeling or advertising other than as approved in the PMA).

particular"[67] or fails to include "adequate information for use."[68] Third, oral statements promoting off-label uses can constitute evidence that the labeling did not contain adequate information for use—a tactic known as the "squeeze play."[69] While FDA's dislike of off-label promotion is well known, judicial receptiveness to FDA's argument that it is always illegal has been somewhat tepid.[70]

B. State Law Claims Against Manufacturers Based on Off-Label Promotion

Plaintiffs injured by on- or off-label uses of drugs and devices can attempt to sue under state law. State law claims based on off-label promotion typically fit into one of three categories: tort, contract, and other state laws such as statutes prohibiting unfair competition and deceptive trade practices.[71]

67. 21 U.S.C. § 352(a)(1).

68. 21 U.S.C. § 352(f). *Accord* 21 C.F.R. §§ 201.100(b)(2)–(5), (c)–(d)(1). *See also* Gail A. Van Norman, *Off-Label Use vs Off-Label Marketing*, 8 JACC: BASIC TO TRANSLATIONAL SCI. 359, 359 (2023) ("It is illegal to promote or advertise use of a drug or device for anything other than its FDA approved use, an act termed 'misbranding.'" (footnotes omitted)).

69. PETER BARTON HUTT, RICHARD A. MERRILL & LEWIS A. GROSSMAN, FOOD AND DRUG LAW: CASES & MATERIALS 927 (5th ed. 2023).

70. *See* Simon, *supra* note 19, at 569–74.

71. *E.g.*, *Frere v. Medtronic, Inc.*, No. EDCV 15-02338, 2016 WL 1533524, at *3, *11 (C.D. Cal. Apr. 6, 2016) (alleging violation of California unfair competition law and Minnesota unlawful trade practices act). Some states have codified all common law products liability actions, often displacing all traditional common law claims. *E.g.*, *Est. of Brown v. Philip Morris Inc.*, 228 F. Supp. 2d 506, 516 (D.N.J. 2002) (holding that New Jersey's Products Liability Act codified common law and "generally subsumes common law product liability claims") (quoting *Repola v. Morbark Indus., Inc.*, 934 F.2d 483, 492 (3d Cir. 1991)).

Tort	Contract	Other
Strict Liability	Breach of Express Warranty	Consumer Protection Statutes[75]
Negligence[72]	Breach of Implied Warranty of Merchantability or	
Fraud-Based Claims[73]	Fitness for a Particular Purpose[74]	
Misuse	Third Party Beneficiary	

Table 1. Summary of Types of State Law Claims against Drug and Device Manufacturers Based on Off-Label Promotion by Claim Type.

Plaintiffs often take a kitchen sink approach to pleading, sometimes alleging more than a dozen different theories of liability. Despite the diversity of potential actions, plaintiffs usually bring products liability-type claims, typically in tort and contract. Products liability in tort and implied warranty claims in contract have a similar thrust.[76] Both examine what information the manufacturer provided to the consumer and how that information shapes a consumer's reasonable use of the product. Incomplete, misleading, or false information may cause a consumer to use a product in a way they did not know was dangerous. Because of the consumer's information asymmetry relative to the manufacturer about the risks and uses of the product, private law holds

72. Negligence claims include negligent representation, warning, design, and manufacturing. *See infra* notes 78–82 and accompanying text.

73. These include representation, inducement, strict liability, and constructive fraud. *E.g.*, *Houston v. Medtronic, Inc.*, 957 F. Supp. 2d 1166, 1178–80 (C.D. Cal. 2013) (analyzing fraudulent misrepresentation, inducement, and strict liability claims); *Schouest v. Medtronic, Inc.*, 92 F. Supp. 3d 606, 612–13 (S.D. Tex. 2015) (constructive fraud claim).

74. Some courts hold these are traditional tort, not contract, doctrines. Helveston, *supra* note 14, at 1105.

75. Some states require plaintiffs to bring traditional tort and contract claims as statutory claims under implied or express warranty theories. For example, Massachusetts does not recognize strict liability claims in tort as such, but rather requires plaintiffs to bring statutory claims under implied or express warranty theories. *Phillips v. Medtronic, Inc.*, 754 F. Supp. 2d 211, 216 (D. Mass. 2010) (citing *Commonwealth v. Johnson Insulation*, 682 N.E.2d 1323, 1326 (Mass. 1997)).

76. They are not identical, however. For a discussion of the differences and why they matter, see Helveston, *supra* note 14, at 1137–43.

the manufacturer liable to induce their production of better information or a better product.

Drug and device manufacturers facing these claims can require courts to analyze whether federal law preempts them by asserting the doctrine as an affirmative defense. But because certain issues in the preemption analysis may turn on specific claims,[77] a more complete understanding requires some explanation of each type of claim within tort and contract.

Tort claims typically fall into three categories: defects in manufacturing, marketing, and design.[78] Manufacturing defect claims allege that the product was not manufactured to specifications. Marketing defects are also called "failure to warn" claims because they typically assert that the manufacturer failed to provide adequate warnings about the risks of using the product.[79] Because of the "learned intermediary doctrine," the duty to warn generally runs from the manufacturer to the physician, not the patient.[80] Design defect claims are about the safety of the product when used. In some jurisdictions, this question is determined by reference to consumer expectations about the use; in others, the

77. *See infra* Sections II.C.1–2.

78. *E.g.*, *McGee v. Johnson & Johnson*, No. 21-639, 2023 WL 4765454 (W.D. Pa. July 26, 2023) (manufacturing defect); *Oja v. Howmedica, Inc.*, 111 F.3d 782 (10th Cir. 1997) (marketing defect); *Jones v. Medtronic Inc.*, 411 F. Supp. 3d 521 (D. Ariz. 2019), *aff'd*, 830 F. App'x 925 (9th Cir. 2020) (design defect). While these claims traditionally sound in strict liability, failure to warn and design defect claims are closer to negligence than strict liability. And they may be asserted as either strict liability or negligence. *See* James A. Henderson, Jr. & Aaron D. Twerski, *Doctrinal Collapse in Products Liability: The Empty Shell of Failure To Warn*, 65 N.Y.U. L. REV. 265, 271–72 (1990) (noting that "after years of frustration" since the American Law Institute stated that "strict liability applies equally" to manufacturing, marketing, and design defect cases, "many courts have finally . . . declared that . . . strict liability, as applied to generically dangerous product cases, was simply negligence by another name"). Other tort claims also exist, including fraudulent misrepresentation and loss of consortium. *E.g.*, *Schouest v. Medtronic, Inc.*, 92 F. Supp. 3d 606 (S.D. Tex. 2015) (fraudulent misrepresentation); *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 320–21 (2008) (loss of consortium).

79. This Article uses "failure to warn" and "marketing defect" interchangeably despite the fact that they may in some cases refer to different causes of action (depending on jurisdiction) sounding in different theories (negligence versus strict liability).

80. *See Simon v. Wyeth Pharms., Inc.*, 989 A.2d 356, 368 (Pa. Super. Ct. 2009). The three limited exceptions to this rule are (1) contraceptives, (2) mass vaccine campaigns, and (3) drugs advertised directly to consumers, though this third exception applies only in New Jersey and has been rejected everywhere else that has considered it. Elise N. McQuain, *The Learned Intermediary Doctrine: An Update*, FROST BROWN TODD ATT'YS (Dec. 19, 2018), https://frostbrowntodd.com/the-learned-intermediary-doctrine-an-update/ [https://perma.cc/4LGX-Y4UD].

question is determined by a risk-utility balancing test.[81] And while these claims sound in strict liability, they also have a basis in negligence. Design and marketing defect claims often incorporate, if not merge with, negligence claims.[82]

Claims in contract involve breach of warranties. These can be express or implied. Express warranties are promises, assurances, or statements the seller affirmatively makes to the buyer about the goods it sells.[83] A firm that sells eyedrops and promises that they will "safely improve your vision by fifty percent," for instance, expressly warrants that the eyedrops will safely improve your vision by fifty percent. If the eyedrops do not improve your vision or actively harm you, the firm is liable in contract for damages.

Breach of implied warranty operates by law rather than some affirmative act by the seller.[84] When selling a product, the law implies certain guarantees related to the product. "Implied warranties" come in two flavors: merchantability and fitness for particular purpose.[85] Both imply duties to the seller based on the buyer's lack of knowledge about the product. The implied warranty of merchantability requires, among other things, that goods be "fit for the ordinary purposes for which such goods are used," "adequately contained, packaged, and labeled," and "conform to the promise or affirmations of fact made on the container or label if any."[86] The implied warranty for a particular purpose, by contrast, requires that the goods are fit for a specific purpose.[87] This warranty applies, however, only in cases where the buyer relies on the seller's informationally superior position to learn how to use the product.[88]

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81. *See* Mike McWilliams & Margaret Smith, *An Overview of the Legal Standard Regarding Product Liability Design Defect Claims and a Fifty State Survey on the Applicable Law in Each Jurisdiction*, IADC PROD. LIAB. COMM. NEWSL., Sept. 2014, at 1, *reprinted in* 82 DEF. COUNS. J. 80, 81 (2015).

82. *See* Henderson & Twerski, *supra* note 78, at 271–73. A firm dividing line can be drawn conceptually between these two categories of torts, but it is difficult to maintain in practice. In design defect cases, this is obvious because when courts are asked to balance the risk and utility of the product, they necessarily must ask themselves questions about the probability and gravity of harm. It is perhaps less obvious in warning cases, but even here courts are reluctant to impose warning requirements on defendants when they could not have known of the risk. *See id.* at 271–75.

83. U.C.C. § 2-313 (AM. L. INST. & UNIF. L. COMM'N 1949).

84. *See, e.g.*, U.C.C. § 2-314 cmt. 2 (noting that "[t]he responsibility imposed" by the implied warranty of merchantability "rests on any merchant-seller").

85. U.C.C. §§ 2-314–15.

86. U.C.C. § 2-314(2).

87. U.C.C. § 2-315.

88. U.C.C. § 2-315.

Although these types of claims may be similar, each of these claims has different pleading requirements that are satisfied through different means. For example, negligence requires the manufacturer exercise a reasonable standard of care while warranty claims focus on particular statements made to the buyer and the particular facts and circumstances surrounding the sale and use of the product.[89] Other claims in tort, such as those for fraud or fraudulent misrepresentation, focus on how the wrongdoer withholds specific knowledge, rather than just on the reasonableness of their actions.[90] Here the law imposes heightened pleading requirements that makes bringing claims challenging, particularly before the parties conduct any discovery.[91] And third-party beneficiary claims are rarer because they require a contract between two parties that benefited a third.[92]

Despite the diversity of claim types, they all hinge on whether the FDCA preempts them. The next Part explains preemption and how courts apply it to drugs and devices.

II. PREEMPTION

Lawsuits against drug and device manufacturers for both on- and off-label uses have traditionally had to confront an important and often determinative question: Are the claims preempted by federal law?[93] If

89. *See* Helveston, *supra* note 14, at 1103–10.

90. *See* RESTATEMENT (SECOND) OF TORTS §§ 525–30 (AM. L. INST. 1977).

91. FED. R. CIV. P. 9(b). *See, e.g.*, *Shuker v. Smith & Nephew, PLC*, 885 F.3d 760, 778 (3d Cir. 2018); *Lempa v. Eon Labs, Inc.*, No. 18 C 3821, 2019 WL 1426011, at *5 (N.D. Ill. Mar. 29, 2019) (quoting *Squires-Cannon v. Forest Pres. Dist. of Cook Cnty.*, 897 F.3d 797, 805 (7th Cir. 2018) (cleaned up)) (Illinois law); *Tutwiler v. Sandoz Inc.*, No. 16-cv-01246, 2017 WL 11609669, at *4 (N.D. Ala. Mar. 9, 2017).

92. *See Mendez v. Shah*, 28 F. Supp. 3d 282, 300 (D.N.J. 2014) ("The Federal government and Medtronic (formerly known as Kyphon, Inc.) entered into a 'Corporate Integrity Agreement' (CIA) to 'promote Kyphon's compliance with . . . Medicare, Medicaid, and all other Federal health care programs.' This agreement was entered into, along with a settlement agreement, to resolve a lawsuit brought against Medtronic based on the Federal government's investigation of Medtronic's submission of false claims to Medicare. Plaintiff asserts that as a Medicare beneficiary, she is also a third party beneficiary to the CIA."); *id.* ("The essence of contract liability to a third party is that the contract be made for the benefit of said third party within the intent and contemplation of the contracting parties." (quoting *Gold Mills, Inc. v. Orbit Processing Corp.*, 297 A.2d 203 (N.J. Super. Ct. Law Div. 1972))).

93. Preemption is most commonly operationalized as an affirmative defense. But cases differ on how to apply preemption, either on what evidence is required to plead facts sufficient to defeat preemption, *see infra* cases cited note 119, or whether preemption is an affirmative defense whose burden rests with the defendant. *Compare Wolicki-Gables v. Arrow Int'l, Inc.*, 634 F.3d 1296, 1299–302 (11th Cir. 2011) (finding that, because plaintiff failed to provide sufficient facts alleging a violation of a parallel

they are, the lawsuit is over; if not, the lawsuit can proceed on state law theories.[94] This Part lays the groundwork for the theory of off-label preemption by explaining how preemption works. Section II.A briefly reviews preemption. Section II.B describes the preemption frameworks that apply to claims against device and drug manufacturers for claims where the manufacturer does not promote off-label uses. Section II.C then explains how courts have applied these frameworks to state law claims against device and drug manufacturers that are based on off-label promotion.

Although somewhat extended, the discussion in this Part is necessary to draw out just how confused and complicated approaches to preemption are, and the need for a theory that can unify them using existing doctrine. Yet once the complexity and doctrinal divisions come into view, the approval theory in Part III is able to push them neatly to one corner. In short, seeing the complete scope of doctrinal confusion and complexity is necessary to appreciate both the need for a unifying theory and the simplicity of the one proposed in this Article.

A. Preemption

Under the doctrine of preemption,[95] federal law displaces (and cancels out) state law when either the federal statute expressly or impliedly dictates. Express preemption occurs when Congress uses express language to displace state law with federal law, like it did with medical devices.[96] Implied preemption occurs when the statute does not contain express preemption language, but there is another reason for state law to give way.[97]

Implied preemption falls into two types: One, called conflict preemption, occurs when simultaneously complying with state and federal law is impossible[98] or creates an obstacle to furthering the federal

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claim, the state common law claims were preempted), *with Wyeth v. Levine*, 555 U.S. 555, 573 (2009) (concluding that "[i]mpossibility pre-emption is a demanding defense"). This Article does not address this question in detail but notes that preemption is best construed as an affirmative defense for which the defendant bears the burden of proof.

94. How far a lawsuit proceeds depends on the merits of the claims.

95. This doctrine is derived from the Supremacy Clause of the U.S. Constitution. U.S. CONST. art. VI, para. 2. *See Cipollone v. Liggett Grp., Inc.*, 505 U.S. 504, 516 (1992). For an alternative view, see Stephen A. Gardbaum, *The Nature of Preemption*, 79 CORNELL L. REV. 767, 770–71 (1994).

96. *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 316 (2008).

97. *See, e.g.*, *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 348 (2001).

98. Sometimes called "impossibility preemption." *E.g.*, *Wyeth*, 555 U.S. at 573.

scheme between the two.[99] The other, called field preemption, arises when Congress, as evidenced by the pervasiveness of regulation, has evinced an intent to regulate a field so extensively as to put state lawmakers out of business.[100]

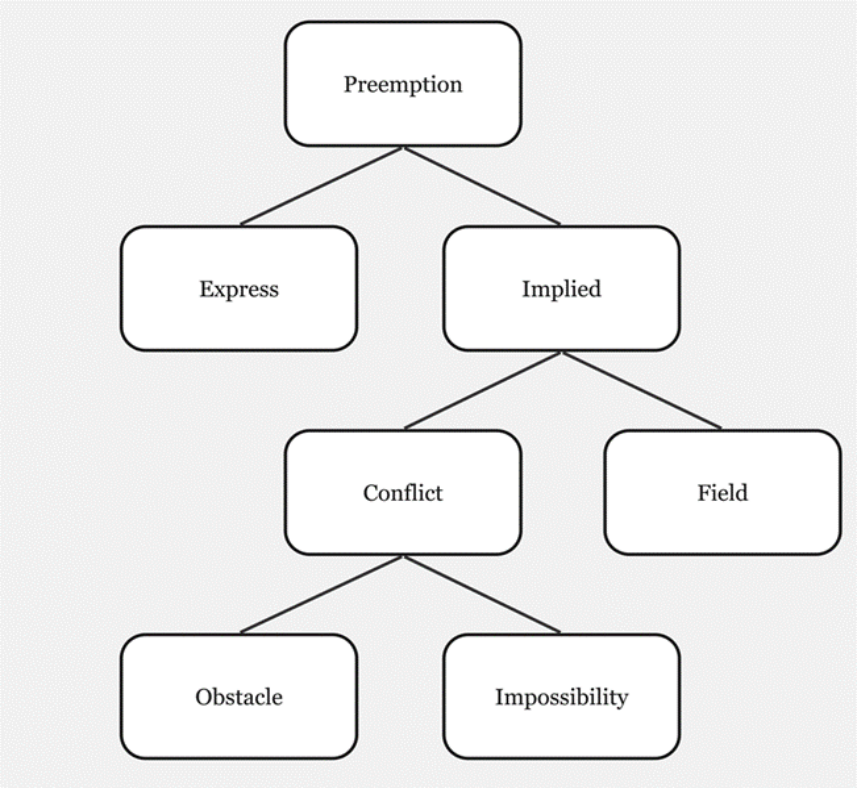

Figure 1. Kinds and Types of Preemption.[101]

Each type of preemption has a distinct inquiry, though all types are fundamentally concerned with evaluating congressional purpose. Express preemption is more like an exercise in statutory interpretation than

99. This is also called "obstacle" preemption. *E.g.*, *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941).

100. *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 507–08 (1996) (describing "field" preemption); Epstein, *supra* note 14, at 55. It is, of course, possible for Congress to expressly preempt an entire field of regulation, but the term "field preemption" refers to a term of art, a specific type of implied preemption.

101. Figure 1 is adapted from CONG. RSCH. SERV., FEDERAL PREEMPTION: A LEGAL PRIMER 3 (2023), https://sgp.fas.org/crs/misc/R45825.pdf [https://perma.cc/FBW6-584V].

implied preemption.[102] The former asks a court to determine the scope of a preemption provision; the latter asks a court to evaluate whether the statutory structure and function reveal anything about whether state law claims can proceed.

B. On-Label Preemption

While claims against drugs and devices fall within the conflict preemption framework, different kinds of preemption (express and implied) apply to products (drugs and devices) for harms that occur from particular uses (on-label or off-label).[103] Claims against device manufacturers, for example, may be expressly or impliedly preempted (by conflict) while claims against drug manufacturers may be only impliedly preempted (by conflict). This Section reviews these differences with respect to state law claims alleging that a drug or device caused their injuries, typically based on an on-label use.[104] For simplicity, it discusses marketing and design defect claims, but the analysis is also applicable to other tort, contract, and state law claims.

1. DEVICES: EXPRESS AND IMPLIED PREEMPTION

State law claims against device manufacturers may be either expressly or impliedly preempted. Express preemption may apply because the Medical Device Amendments (MDA)[105]—the federal law governing device regulation—contains a preemption provision.[106] Under the MDA, states cannot impose "requirements" relating to "the safety or effectiveness of the device or to any other matter included in a

102. *Riley v. Cordis Corp.*, 625 F. Supp. 2d 769, 783 (D. Minn. 2009) ("[I]mplied preemption . . . involves weighing policy considerations; the 'pros' and 'cons' of preemption are weighed by the court. . . . [E]xpress preemption . . . involves interpreting the words of a statute; the 'pros' and 'cons' have already been weighed by Congress.").

103. Table 4, *infra*, seeks to correct judicial conflations between kinds and types of preemption. *Cf., e.g.*, *Stengel v. Medtronic Inc.*, 704 F.3d 1224, 1230–31 (9th Cir. 2013) ("There are three categories of preemption: express, field, and conflict.").

104. The distinction between on- and off-label preemption is not entirely accurate. The distinction is really between preemption of claims where the manufacturer did not evince an objective intent that the drug or device be used off label (*i.e.*, on-label use) and those where it did (*i.e.*, off-label use). For convenience, however, this Article uses the terms on- and off-label preemption.

105. Medical Device Amendments of 1976, Pub. L. No. 94-295, 90 Stat. 539.

106. 21 U.S.C. § 360k(a).

requirement applicable to the device" that are "different from, or in addition to," federal "requirement[s] under [the FDCA]."[107]

To determine whether this provision applies to state law claims, courts ask three questions.[108] First, is there a federal requirement applicable to the device? Second, does the federal requirement relate to the safety and effectiveness of the device? Third, is there a state law requirement applicable to the device that is different from or in addition to the federal one?[109] If the answer to all three questions is yes, the claims are expressly preempted.[110] If, however, the answer to any of these questions is no, the claims are not expressly preempted. Since in most cases the alleged requirements relate to the safety and effectiveness of a device, this Section will not address that question in detail.

The answer to the first question depends on the regulatory pathway through which the device reached the market. For riskier devices that go through the most extensive review—PMA—the answer is yes.[111] But for less risky devices that are not reviewed or go through the less stringent 510(k) pathway,[112] the answer is no.[113] In other words, federal law imposes "requirements" on PMA devices but not 510(k) devices.[114]

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107. *Id. See also* Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–399i. The MDA allows state and local governments to apply for an exemption from the statute's preemption provision. 21 U.S.C. § 360k(b); 21 C.F.R. § 808.1. FDA has also clarified the types of state requirements that are not preempted. 21 C.F.R. § 808.1(d). FDA has approved this exemption for only hearing aid products. 21 C.F.R. § 808.53. California's recent attempt to obtain exemptions for several devices, including for ophthalmologic devices, was denied. 21 C.F.R. § 801.55 (Aug. 17, 2022). Other states have been similarly denied exemptions in the past. *E.g.*, 45 Fed. Reg. 67336 (Oct. 10, 1980).

108. *See, e.g.*, *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 321–22 (2008).

109. *See id.*

110. *See id.* at 321–25.

111. *See id.* at 317 ("Although the MDA established a rigorous regime of premarket approval for new Class III devices . . . . [d]evices sold before the MDA's effective date may remain on the market until the FDA promulgates . . . a regulation requiring premarket approval.").

112. Strictly speaking, the fact that a device goes through 510(k) review rather than PMA review does not *necessarily* mean that the former is less risky than the latter as an empirical matter. *See id.* ("A new device need not undergo premarket approval if the FDA finds it is 'substantially equivalent' to another device exempt from premarket approval."). But in general, the 510(k) review is reserved for intermediate risk devices. *FDA 510(k) Explained: A Basic Guide to Premarket Notification*, FDA GRP., LLC (Mar. 23, 2023), https://www.thefdagroup.com/blog/510k-explained [https://perma.cc/XV9M-H7D5].

113. *See, e.g.*, *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 492–94 (1996).

114. *Id. See also id.* at 513 (O'Connor, J., concurring and dissenting in part) (noting, however, that it *agrees* with the majority that the design claim is not preempted because 510(k) does not impose federal requirements). Five justices held that state common law cause of action imposed requirements under state law, and four held it did

According to the Supreme Court, requirements imposed by the 510(k) process—requirements relating to labeling, misbranding, adulteration, and manufacturing regulation—are "general,"[115] while those imposed by the PMA process are "specific to individual devices."[116] General requirements are unlikely to trigger the express preemption provision because they express "generic concerns" over device regulation.[117] Specific requirements however, evince a government's consideration of a federal interest in a particular case by imposing a corresponding duty on manufacturers to effectuate it.[118] Underpinning this conclusion is a determination that the 510(k) process is concerned with "*equivalence*, not safety."[119] Because federal requirements apply only to PMA-devices and not those cleared through the 510(k) process, federal law expressly preempts only state law claims against PMA-devices.

Answering the third question is both more straightforward and less certain. Although state law duties like those found in tort and contract constitute "requirements" applicable to the device,[120] not all requirements will be "different from, or in addition to," those under the MDA.[121] The crucial question, therefore, is whether state law requirements are different from, or in addition to, the federal ones.

Broadly speaking, state law claims that allege standard marketing and design defect claims are preempted because they conflict with FDA's risk evaluation function.[122] Imposing tort duties to warn of dangers FDA

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not by distinguishing the Court's holding in *Cipollone*. *Id.* at 486–91 (plurality opinion). Justice Breyer wrote a concurring opinion calling this into question. *Id.* at 504–05 (Breyer, J., concurring in part and concurring in the judgment). *Id.* at 509–13. In *Riegel*, the Court adopted the view that general state law duties are state "requirements" under the MDA. *Riegel*, 552 U.S. at 323–24. For an argument that this approach is wrong, see Vladeck, *supra* note 14.

115. *See Lohr*, 518 U.S. at 501–02.

116. *Riegel*, 552 U.S. at 322–23.

117. *See id.* at 322 (quoting *Lohr*, 518 U.S. at 501).

118. *Lohr*, 518 U.S. at 501.

119. *Id.* at 492–93 (quoting *Lohr v. Medtronic, Inc.*, 56 F.3d 1335, 1348 (11th Cir. 1995).

120. *Riegel*, 552 U.S. at 323–34.

121. *See id.* at 333–34, 344–45 (Ginsburg, J., dissenting) (citing 21 U.S.C. § 360k(a)(1)).

122. *See, e.g.*, *In re Medtronic, Inc., Sprint Fidelis Leads Prods. Liab. Litig.*, 623 F.3d 1200, 1206 (8th Cir. 2010) (explaining that design defect claims are not parallel and preempted because they are "attacks on the risk/benefit analysis that led the FDA to approve an inherently dangerous Class III device"); *Jones v. Medtronic*, 89 F. Supp. 3d 1035, 1051–52 (D. Ariz. 2015) (dismissing design and failure to warn defect claims as preempted), *aff'd in part, vacated in part*, 745 F. App'x 714 (9th Cir. Aug. 16), *amended on denial of reh'g* (9th Cir. Sept. 7, 2018) (affirming holding that the design defect claim was preempted); *Burrell v. Bayer Corp.*, 260 F. Supp. 3d 485, 494 (W.D.N.C. 2017)

reviewed during approval or to design a product differently than the one approved, would undermine the system of regulatory review.[123] Put differently, these claims would second guess FDA's risk determination and impose requirements over and above what federal law requires.

That said, not all state law duties are different from or in addition to federal ones. Where state law duties "parallel" federal ones, they can form the basis of a state law claim.[124] For example, a state law claim for a manufacturing defect that is based on a violation of FDA manufacturing guidelines can sometimes proceed without running into a wall of preemption.[125] The reason is because the state law manufacturing defect claim covers the same conduct as a violation of FDA regulations.[126] In short, "parallel claims" against manufacturers of PMA devices are *not* expressly preempted.[127]

Regardless of whether express preemption applies, federal law may *impliedly* preempt state law claims that allege no more than violations of federal law—so-called "fraud-on-the-FDA" claims.[128] To avoid implied preemption, the Supreme Court held in *Buckman Co. v. Plaintiffs' Legal Committee*,[129] state law claims must contain some allegation that the manufacturer violated an independent, traditional state law that "predate[s] the federal enactments."[130] For example, federal law would preempt a state law claim that alleged a manufacturer provided fraudulent information to FDA about how it intended to use the device during the

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(explaining that the design defect claim was preempted under MDA because "the FDA made its determination of this products safety and effectiveness for its given use").

123. *Compare Williams v. Bayer Corp.*, 541 S.W.3d 594, 604 (Mo. Ct. App. 2017) (reasoning implied warranty of fitness for ordinary purpose claim was preempted because it "directly contradicts the FDA's determination that Essure is a safe and effective means of birth control"), *with id.* at 606–07 (holding tort claims of strict liability and negligent manufacturing were not preempted because the claims "her claims do not simply stand on the premise that her device was not manufactured in conformance with the Essure PMA, . . . but go on to assert state law based causes of action that exist independent of such violations").

124. *Riegel*, 552 U.S. at 330.

125. *Williams*, 541 S.W.3d at 606–07. Some courts have also held that failure to warn claims run parallel to failing to report adverse events, even for PMA devices. *See Hughes v. Bos. Sci. Corp.*, 631 F.3d 762, 770 (5th Cir. 2011).

126. *See Riegel*, 552 U.S. at 330.

127. *Id.* ("Thus, § 360k does not prevent a State from providing a damages remedy for claims premised on a violation of FDA regulations; the state duties in such a case 'parallel,' rather than add to, federal requirements."). *See also Medtronic, Inc. v. Lohr*, 518 U.S. 470, 495 (1996).

128. *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 348 (2001).

129. *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341 (2001). The *Buckman* Court held that the claims were impliedly preempted under obstacle preemption. *Id.* at 348–49.

130. *Id.* at 353.

approval or clearance process. By contrast, a claim that the manufacturer should have sought approval for new risks it knew or should have known about is not necessarily impliedly preempted.

Preemption analysis is therefore a multi-step process involving different decision frameworks, as depicted in Figure 2.

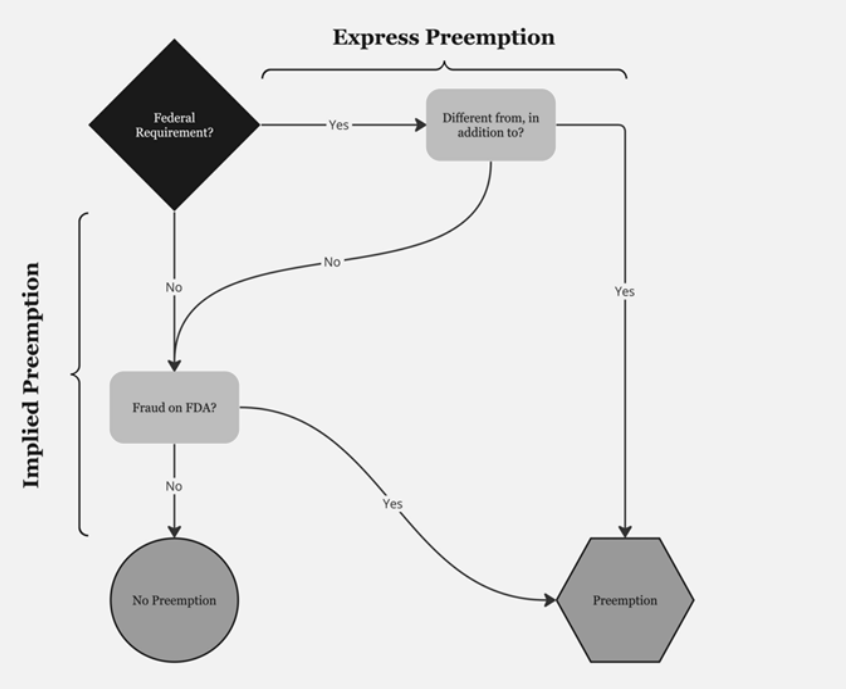

Figure 2. Decision Tree for Express and Implied Preemption of Claims against PMA Device Manufacturers.

The upshot is the framework depicted in Table 3. For PMA devices, express preemption applies to all but parallel claims and implied preemption applies to fraud-on-the-FDA claims. This leaves a rather narrow band of claims that mainly focus on manufacturing and marketing defect claims.[131] Navigating this "narrow gap"[132] requires the plaintiff to allege *both* that the defendant violated FDA regulations *and* that the claim

131. *See, e.g.*, *In re Medtronic, Inc., Sprint Fidelis Leads Prods. Liab. Litig.*, 623 F.3d 1200, 1205–06 (8th Cir. 2010).

132. *Id.* at 1204 (quoting *Riley v. Cordis Corp.*, 625 F. Supp. 2d 769, 777 (D. Minn. 2009)); *Perez v. Nidek Co.*, 711 F.3d 1109, 1120 (9th Cir. 2013) (quoting *In re Medtronic*, 623 F.3d at 1204); *Jones v. Medtronic, Inc.*, 745 F. App'x 714, *716 (9th Cir.), *as amended on denial of reh'g* (Sept. 7, 2018); *Brooks v. Mentor Worldwide LLC*, 985 F.3d 1272, 1276 (10th Cir. 2021).

does not "exist *solely* by virtue" of the federal violation.[133] In other words, "[t]he plaintiff must be suing for conduct that *violates* the FDCA, . . . but the plaintiff must not be suing *because* the conduct violates the FDCA."[134] Although express and implied preemption are distinct concepts, most courts analyze implied preemption when discussing the third prong of express preemption (whether state law claims add to or differ from federal law).[135]

For 510(k) devices, express preemption does not apply but implied preemption may. Claims against manufacturers of 510(k) devices can therefore include design defect claims in addition to marketing and manufacturing defect claims.

133. *Buckman*, 531 U.S. at 352–53 (emphasis added). Unlike implied preemption, discussed below, under express preemption courts typically hold that to be a federal requirement on which a parallel claim is premised, the federal obligation must be mandatory rather than permissive. *See, e.g.*, *Brooks*, 985 F.3d at 1280.

134. *Bausch v. Stryker Corp.*, 630 F.3d 546, 557–58 (7th Cir. 2010) (quoting *Riley*, 625 F. Supp. 2d at 777). *See also* 21 U.S.C. § 360c(f)(2); 21 C.F.R. subpart D (2024).

135. *See, e.g.*, *Martin v. Medtronic, Inc.*, 32 F. Supp. 3d 1026, 1033–38 (D. Ariz. 2014). These claims will frequently be decided together because plaintiffs must allege some state law duty to bring a claim. The third prong of express preemption will ask whether the state law duty is different from or in addition to federal requirements. Implied preemption will ask whether the duty actually exists under state law. But for all practical purposes, the first question cannot be answered without supposing a state law duty exists. The cases where the duty is based wholly on federal law are quite limited. *See, e.g.*, *Stengel v. Medtronic Inc.*, 704 F.3d 1224, 1227–34 (9th Cir. 2013) (discussing implied preemption by reference to state law duties articulated during the express preemption analysis).

FDA Review	**Preemption Type**	**Claim Type Preempted**		
Pathway	*Express or Implied*	Fraud-on-FDA	Parallel	Other State Law
PMA	Express and Implied	Yes	No	Yes
510(k)	Implied	Yes	No	No
De Novo*	Implied (presumably)	Yes (presumably)	No (presumably)	No (presumably)
Exempt	Implied	Yes	No	No

*De novo review—a pathway for devices with low to moderate risk but do not qualify for the 510(k) pathway[136]—has not yet been the subject of a preemption analysis. Given that it is designed to provide a 510(k)-like process for new devices, however, it is reasonable to assume preemption analysis for devices authorized under the de novo review would be the same (or substantially the same) as those cleared through the 510(k) process.

Table 2. Express and Implied Preemptive Effect of MDA on Tort Claims against Device Manufacturers by Claim Type.

In summarizing the broad outlines of the preemption frameworks, Table 2 necessarily glosses over doctrinal schisms that have developed among the courts. To give one example, courts have disagreed about whether FDA regulations on good manufacturing practices constitutes specific federal requirements that trigger express preemption.[137] Courts

136. 21 U.S.C. § 360c(f)(2)(A); 21 C.F.R. subpart D (2024).

137. *Compare, e.g.*, *In re Medtronic, Inc. Sprint Fidelis Leads Prods. Liab. Litig.*, 592 F. Supp. 2d 1147, 1157 (D. Minn. 2009), *aff'd*, 623 F.3d 1200 (8th Cir. 2010) (holding that FDA's regulations on good manufacturing practices and quality system review "are simply too generic, standing alone, to serve as the basis for Plaintiffs' manufacturing-defect claims"), *and In re Medtronic, Inc., Sprint Fidelis Leads Prods. Liab. Litig.*, 623 F.3d 1200, 1205–06 (8th Cir. 2010) (holding that general allegations that defendant violated MDA not sufficient to state a parallel design defect claim), *with Frere v. Medtronic, Inc.*, No. EDCV 15-02338, 2016 WL 1533524, at *7 (C.D. Cal. Apr. 6, 2016) ("While 'CGMPs typically set forth open-ended standards, not concrete requirements,' the FDA's application of CGMPs to Defendants, as alleged in Plaintiff's FAC, are not as 'vague and open-ended' as Defendants describe.").

also have differing views on what constitutes a parallel claim,[138] as well as how to evaluate combination products (where a product is some combination of drugs, devices, and biologics).[139] And an open question remains as to how it applies to hybrid devices (where a cleared or approved device contains components that were separately cleared or approved).[140]

2. DRUGS: IMPLIED PREEMPTION

Unlike the MDA, the FDCA contains no express preemption provision applicable to prescription drugs.[141] Therefore, federal law never expressly preempts state law claims against drug manufacturers. Because federal drug law and state law claims against drug manufacturers can still conflict, however, implied preemption may apply even when express preemption does not.

The general rule comes from *Wyeth v. Levine*,[142] which held that preemption does not apply to state law marketing defect claims that allege the manufacturer failed to update its label to reflect new risk information under FDA's so-called "changes being effected" (CBE) regulations.[143]

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138. *Compare, e.g.*, *Burkett v. Smith & Nephew Gmbh*, No. CV 12-4895, 2014 WL 1315315, at *5 (E.D.N.Y. Mar. 31, 2014) ("[A] parallel claim may not be predicated on alleged violation of CGMPs . . . ."), *and Ilarraza v. Medtronic, Inc.*, 677 F. Supp. 2d 582, 588 (E.D.N.Y. 2009) (same), *with Bausch*, 630 F.3d at 552–53 (finding manufacturing defect claim was parallel and not expressly preempted), *and Howard v. Sulzer Orthopedics, Inc.*, 382 F. App'x 436, *440 (6th Cir. 2010) (rejecting application of *In re Medtronic*, 592 F. Supp. 2d 1147, to the alleged violations in *Howard*). *See also Lamere v. St. Jude Med., Inc.*, 827 N.W.2d 782, 790 (Minn. Ct. App. 2013) (discussing how "federal circuit courts are split as to whether federal GMPs may form the basis of a parallel claim").

139. *See, e.g.*, *Riley*, 625 F. Supp. 2d at 780 ("It makes no sense—indeed, it would probably be impossible—to pick apart the components of a medical device and apply different preemption analyses to different components.").

140. *See, e.g.*, *Shuker v. Smith & Nephew, PLC*, 885 F.3d 760, 772 (3d Cir. 2018) ("[A]nalysis at the component level is the only way to harmonize various provisions of the statute."); *Bennington v. Stryker Corp.*, No. 20-cv-01211, 2023 WL 4136656, at *5–6 (D. Colo. June 22, 2023) (following *Shuker* and finding that individual devices (510(k) and PMA) were not a hybrid device when used together and that PMA protections did not apply to the 510(k) devices because the PMA did not include the 510(k) or any device similar to it as a component of the PMA system). *See also White v. Medtronic, Inc.*, 808 F. App'x 290, *294–95 (6th Cir. 2020) (finding preemption applied to components of a hybrid device when only one component of the device was used in the off-label context).

141. *But see* 21 U.S.C. § 379r(a) (express preemption provision for over-the-counter drugs).

142. 555 U.S. 555 (2009).

143. *Id.* at 558–59, 568. *Wyeth* found neither obstacle nor impossibility preemption applied. *Id.* at 571–73 (impossibility); *id.* at 573–81 (obstacle). Until 2008

The CBE regulations allow a brand name drug manufacturer to unilaterally add or strengthen warnings on the label based on "newly acquired information" and submit it to FDA for review.[144] *Buckman* does not bar these claims since failing to update the label under the CBE regulations generally can be tied to marketing defect (implied warranty, and fraud) claims, which are premised on a state law duty to warn consumers about the risks of their products.[145] Practically, this means that

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(and hence at issue in *Wyeth*), the regulations provided that the drug manufacturer can unilaterally change its label by filing a supplemental application with FDA to "add or strengthen a contraindication, warning, precaution, or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product." 21 C.F.R. §§ 314.70(c)(6)(iii)(A), (C) (2007). In 2008, the FDA issued a new rule that changed the type of information that could be used to update the label using the CBE regulation. First, it stated that the regulation could be used "[t]o add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter." Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 49603, 49609 (Aug. 22, 2008) (codified at 21 C.F.R. § 314.70(6)(c)(iii)(A) (2024)). Second, it defined "newly acquired information" to mean data, analyses, or other information not previously submitted to the agency, which may include (but are not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA. *Id.* (codified at 21 C.F.R. § 314.3(b)). Drug manufacturers can make changes to the drug label through two other means but not unilaterally. *See* 21 C.F.R. § 314.70(b) (Prior Approval Supplement); 21 U.S.C. § 355(o) (codification of FDA-initiated proposed change under 2007 amendments).

144. *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1679 (2019) ("[C]ourts should treat the critical question not as a matter of fact for a jury but as a matter of law for the judge to decide. And where that is so, the judge must simply ask himself or herself whether the relevant federal and state laws 'irreconcilably conflic[t].'" (quoting *Rice v. Norman Williams Co.*, 458 U.S. 654, 659 (1982))).

145. *See, e.g.*, *In re: Zofran (Ondansetron) Prods. Liab. Litig.*, 541 F. Supp. 3d 164, 195 (D. Mass. 2021) *aff'd*, 57 F.4th 327 (1st Cir. 2023); *Pfaff v. Merck & Co.*, 627 F. Supp. 3d 134, 143–44 (E.D.N.Y. 2022) (citing *Zofran*, 541 F. Supp. 3d 164). Where a manufacturer has no "newly acquired information," these courts have held that the CBE process is "not . . . available." *Id.* at 144; *Zofran*, 541 F. Supp. 3d at 168. Just how this analysis proceeds is an open question. *Compare Gibbons v. Bristol-Myers Squibb Co.*, 919 F.3d 699, 708 (2d Cir. 2019) (holding that plaintiff must first make an affirmative showing that the manufacturer had "newly acquired information" that enabled a label change, which then shifts the burden to the manufacturer to show FDA would have rejected the labeling change by clear evidence), *with Zofran*, 541 F. Supp. 3d at 196–97 (holding that preemption is an affirmative defense, both for establishing whether it had no newly acquired information and whether FDA would have rejected a proposed CBE label change, on which the manufacturer bears the burden of proof and rejecting *Gibbons*). *See also* Arameh O'Boyle & Clancy Galgay, *"Newly Acquired Information" and Federal Preemption Defenses in Pharmaceutical Products Liability Cases*, ABA: PRAC. POINTS (July 19, 2019) [https://perma.cc/746T-NH4B?type=standard] (urging

failure to warn claims based on "newly acquired information"[146] can proceed unless the manufacturer shows by "clear evidence that the FDA would not have approved a change."[147]

Determining whether FDA issued an "agency action" by rejecting a labeling change, the Court clarified in *Merck Sharp & Dohme Corp. v. Albrecht*,[148] requires a *legal* rather than factual assessment.[149] To do this, the "judge must simply ask himself or herself whether the relevant federal and state laws 'irreconcilably conflic[t].'"[150] As part of this legal inquiry courts may consider subsidiary factual disputes about, for example, what information the FDA used to make its decision.[151] This decision shut the door on preemption in some courts that interpreted *Wyeth* as requiring a judicial evaluation of what FDA, hypothetically, would have done had it considered new information.

While *Wyeth* and *Albrecht* saved some failure to warn claims, they did not save them all. In *PLIVA, Inc. v. Mensing*,[152] the Court refused to extend *Wyeth* to generic manufacturers, holding that impossibility preemption foreclosed failure to warn claims against them.[153] The reasoning went like this: FDA regulations require generic manufacturers to have identical labeling to the brand manufacturer. State law duties imposed by failure to warn claims would require generics update their label, violating federal law. It was impossible, therefore, for a

courts to "[reaffirm] plaintiffs' burden to demonstrate that 'newly acquired information' existed such that the CBE was a viable option to update the label").

146. 21 C.F.R. § 314.3(b).

147. *Wyeth*, 555 U.S. at 571. For the confusion this wrought, see Eric Lindenfeld, *Clear Evidence Clarified*, 75 FOOD & DRUG L.J. 346 (2020); Michael M. Gallagher, *Clear Evidence of Impossibility Preemption After* Wyeth v. Levine, 51 GONZ. L. REV. 439 (2016).

148. 139 S. Ct. 1668 (2019). *Albrecht* laid down several other criteria for the test, but they are not relevant to the discussion. *Id.* at 1672 (holding that the initial question before assessing conflict is whether the manufacturer "fully informed the FDA of the justifications for the warning required by state law and that the FDA . . . informed the drug manufacturer that the FDA would not approve a change"); *id.* at 1678. Case law in this area is still developing. *See, e.g.*, *Duncan v. Allergan, Inc.*, No. CV 18-8047, 2020 WL 6204563, at *6 (C.D. Cal. Sept. 4, 2020); *Cerveny v. Aventis, Inc.*, 783 F. App'x. 804, *808 & n.9 (10th Cir. 2019) (upholding preemption decision in light of *Albrecht*); *Dolin v. GlaxoSmithKline LLC*, 951 F.3d 882, 886, 889–91 (7th Cir. 2020) (same).

149. *Albrecht*, 139 S. Ct. at 1679.

150. *Id.* at 1679 (quoting *Rice v. Norman Williams Co.*, 458 U.S. 654, 659 (1982)).

151. *Id.* at 1679–80.

152. 564 U.S. 604 (2011).

153. *Id.* at 624–26. The decision was based on a finding of impossibility preemption. *Id.* at 618–21.

manufacturer to comply with both federal and state law duties simultaneously.[154]

With a narrowing window for failure to warn claims, some plaintiffs have tried pleading design defect claims.[155] Unlike warning defect claims that center on *post-approval* actions (*i.e.*, updating risk information on drug labeling), design defect claims typically hinge on *pre-approval* actions: Could the manufacturer have sought FDA approval for a differently designed (safer) drug instead of the one that injured the

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154. *Id.* at 618 ("[I]t was impossible for the Manufacturers to comply with both their state-law duty to change the label and their federal-law duty to keep the label the same."). *But see* 21 U.S.C. §§ 355(j)(2)(A)(v), (vii)–(viii), (C). Some courts have extended *Mensing*'s rationale to other forms of communication. *E.g.*, *Guarino v. Wyeth, LLC*, 719 F.3d 1245, 1249 (11th Cir. 2013) (preempting applied claim based on "failure to communicate" label changes to pharmacists); *Morris v. PLIVA, Inc.*, 713 F.3d 774, 776–77 (5th Cir. 2013) (per curiam) ("Whether a warning is placed on the label on the bottle or in letters to distributors, any state law duty requiring generic manufacturers to act unilaterally in this area is preempted by federal law.").

155. *See, e.g.*, *Holley v. Gilead Scis., Inc.*, 379 F. Supp. 3d 809, 824 (N.D. Cal. 2019) (holding that pre-approval design defect claims were not preempted after finding compliance with federal and state requirements was not impossible and concluding that, drawing on *Wyeth v. Levine*, 555 U.S 555 (2009), the defendant "ha[d] not presented 'clear evidence' that the FDA would not have approved the allegedly safer versions of the drugs that Plaintiffs contend would have complied with state law"); *Anderson v. Merck & Co., Inc.*, No. 22-cv-02991, 2022 WL 17096157, at *6 (N.D. Cal. Nov. 21, 2022) ("For the reasons articulated in *Holley* and based on the facts before the Court, it concludes Defendants have not demonstrated that Anderson's design defect claims are preempted."); *Gaetano v. Gilead Scis., Inc.*, 529 F. Supp. 3d 333, 343–44 (D.N.J. 2021) (holding that design defect claim against brand name manufacturer was not preempted at the motion to dismiss stage and attempting to distinguish from *Mutual Pharmacy Co. v. Bartlett*, 570 U.S. 472 (2013), on the grounds that the drug there was generic and that required redesign after approval, not before as alleged in this case); *Guidry v. Janssen Pharms., Inc.*, 206 F. Supp. 3d 1187, 1201–09 (E.D. La. 2016) (holding design defect claim against brand name manufacturer not preempted and distinguishing *Yates v. Ortho-McNeil-Janssen Pharma., Inc.*, 808 F.3d 281 (6th Cir. 2015)); *Est. of Cassel v. Alza Corp.*, No. 12-cv-771, 2014 WL 856023, at *5 (W.D. Wis. Mar. 5, 2014) (ruling on a motion for summary judgment that design defect claim against brand name manufacturer not preempted); *Young v. Bristol-Myers Squibb Co.*, No. 16-CV-00108, 2017 WL 706320, at *8 (N.D. Miss. Feb. 22, 2017) (finding persuasive and following *Guidry*); *Brazil v. Janssen Rsch. & Dev. LLC*, 249 F. Supp. 3d 1321, 1348 (N.D. Ga. 2016) (denying a motion to dismiss for design defect claims against brand-name drug company holding them not preempted); *Sullivan v. Aventis, Inc.*, No. 14-cv-2939, 2015 WL 4879112, at *4–5 (S.D.N.Y. Aug. 13, 2015) (holding preemption did not apply to brand-name manufacturer on motion to dismiss and that "[b]rand-name drug manufacturers can thus avoid liability under New York law by choosing a safer design for a drug"); *Trahan v. Sandoz, Inc.*, No. 13-cv-350-J-34, 2015 WL 2365502, at *5–6 (M.D. Fla. Mar. 26, 2015) (holding that a generic drug formulation could have been designed safer because the brand-name manufacturer had recently received approval for a safer formulation of the drug and that the generic could have used that design or even a safer design that complied with the previous brand-name formulation prior to FDA approval of its ANDA).

plaintiff? Although the Court has not squarely addressed this question, its decision in *Mutual Pharmaceutical Co. v. Bartlett*[156] suggests it is likely to find such claims preempted.[157] *Bartlett* involved a design defect claim against a generic manufacturer, which the Supreme Court held to be preempted because the alternative would require generic drugs to "stop selling" and exit the market entirely.[158]

Without a Supreme Court decision on design defect claims against brand manufacturers, state and federal courts considering the issue are mixed. A number have concluded that federal law does not always preempt such claims.[159] Others, however, have held that this is just another version of a "stop-selling" argument the Supreme Court rejected in *Bartlett*.[160] For now, the question remains unresolved.[161]

Manufacturing defect claims, however, can still proceed against all drug manufacturers but require navigating nuanced issues in state and federal law. When properly alleged, these claims are straightforward but are difficult to win because of their demanding requirements.[162]

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156. 570 U.S. 472 (2013).

157. *Id.* at 484.

158. *Id.* at 488–90.

159. *See* cases cited *supra* note 39.

160. *Yates*, 808 F.3d at 300 (holding design defect claim preempted); *Amos v. Biogen Idec Inc.*, 28 F. Supp. 3d 164, 169 (W.D.N.Y. 2014) (holding design defect claims against brand-name manufacturer preempted under *Bartlett* as a matter of law but also noting that "plaintiffs concede that design defect claims are preempted under federal law, and have agreed to withdraw those claims without prejudice"); *Gustavesen v. Alcon Lab'ys, Inc.*, 272 F. Supp. 3d 241, 250–56 (D. Mass. 2017), *aff'd*, 903 F.3d 1 (1st Cir. 2018) (adopting *Yates* and finding preempted a design defect claim that alleged the manufacturer's eye dropper size was too large constituted a "major change" under federal regulations that required submission to the FDA before product distribution but noting that its decision would not preempt claims that require "moderate" or "minor" changes as defined by federal regulations that would avoid deceiving consumers). *See also Silver v. Bayer Healthcare Pharms., Inc.*, No. 19-cv-3495, 2021 WL 4596918, at *11–12 (D.S.C. June 10), *report and recommendation adopted in part, rejected in part*, No. 19-cv-3495, 2021 WL 4472857 (D.S.C. Sept. 30, 2021) (noting the Fourth Circuit has not addressed whether pre-approval design defect claims can proceed but refraining from ruling on the issue pending discovery); *Evans v. Gilead Scis., Inc.*, No. 20-cv-00123, 2020 WL 5189995, at *9 (D. Haw. Aug. 31, 2020) (holding product defect claim for brand name drug preempted on the grounds that a pre-approval defect theory amounts to a "'never-start selling rationale' akin to the 'stopselling rationale' rejected in *Bartlett*").

161. Given the Supreme Court's jurisprudence, it seems likely that it will find design defect claims preempted unless they are parallel claims.

162. *See, e.g.*, *Guidry v. Janssen Pharms., Inc.*, 206 F. Supp. 3d 1187, 1197 (E.D. La. 2016); *Bell v. Boehringer Ingelheim Pharms., Inc.*, No. 17-cv-01153, 2018 WL 928237, at *5–6 (W.D. Pa. Feb. 15, 2018); *Batoh v. McNeil-PPC, Inc.*, 167 F. Supp. 3d 296, 320–22 (D. Conn. 2016).

With the addition of *Mensing* and *Bartlett*, implied preemption jurisprudence for drugs can be divided into two situations, as depicted in Table 3.[163]

On- or Off-Label	Brand or Generic	Claim Type Preempted		
		Manufacturing	*Design*	*Warning*
On-Label	Brand	No	Maybe	Some
On-Label	Generic	No	Yes	Yes

Table 3. Preemption of Tort Claims against Prescription Drug Manufacturers by Claim Type.

For brand name drugs, state law claims are limited to those based on defects in manufacturing, certain kinds of marketing, and possibly some design defect claims. But for generic drugs, it seems likely that claims are limited to manufacturing defect claims.

3. SUMMARY

Drugs and devices are subject to different kinds of preemption. Federal law can expressly or impliedly preempt state law claims against device manufacturers for on-label uses while it can only impliedly preempt state law claims against drug manufacturers for on-label uses. The different preemptive frameworks applicable to drugs and devices mean that preemption has a different scope in each context, as depicted in Table 4.

163. Although Table 3 includes only manufacturing, design, and warning defect claims, it (along with subsequent charts) can be read more broadly. For example, preemption applies to these three warning defect claims in both strict liability and negligence. It also applies to implied warranty claims (of both types) and many state law claims that require certain warnings or disclosures. Excluded specifically are express warranty claims and fraud-based claims, which are often treated differently by courts. *Compare Est. of Cipollone v. Liggett Grp., Inc.*, 505 U.S. 504, 522, 526–30 (1992) (plurality opinion), *with In re Medtronic, Inc., Sprint Fidelis Leads Prod. Liab. Litig.*, 623 F.3d 1200, 1207–08 (8th Cir. 2010) (distinguishing *Cipollone* and finding express warranty claims under MDA expressly preempted), *and Bass v. Stryker Corp.*, 669 F.3d 501, 515 (5th Cir. 2012) (agreeing with *In re Medtronic* that express warranty claims are expressly preempted).

Drug or Device	**FDA Review**	**Preemption Type**	**Claim Type Preempted**		
	Pathway	*Express or Implied*	Fraud-on-FDA	Parallel	Other State Law
Devices	PMA	Express & Implied	Yes	No	Yes
	510(k)	Implied	Yes	No	No
	De Novo*	Implied (presumably)	Yes (presumably)	No (presumably)	No (presumably)
	Exempt	Implied	Yes	No	No
Drugs	Standard	Implied	Yes	Some	Some
	Accelerated†	Implied	Yes (presumably)	Some (presumably)	Some (presumably)
	ANDA (generics)	Implied	Yes	Maybe	Yes

* De novo review—a pathway for devices with low to moderate risk that do not qualify for the 510(k) pathway—has not yet been the subject of a preemption analysis. Given that it is designed to provide a 510(k)-like process for new devices, however, it is reasonable to assume preemption analysis for devices authorized under the de novo review would be the same (or substantially the same) as those cleared through the 510(k) process.

† No drug that reached the market through accelerated approval pathway has yet been the subject of a personal injury lawsuit.[164]

Table 4. Express and Implied Preemption of Tort Claims against Drug and Device Manufacturers for On-Label Uses by Claim Type.

Preemption operates more broadly to claims against PMA devices than to 510(k) devices. And it operates more broadly as to claims against generic drug manufacturers than brand name drug manufacturers.

Two pathways to market have not yet been tested for their preemptive effect. Novel devices that present a low risk can reach the market through the de novo review, which is less extensive than PMA.[165] And drugs that treat serious conditions and fill an unmet medical need

164. This conclusion is based on my review of all cases in Westlaw and Lexis involving drugs that received accelerated approval.

165. 21 U.S.C. § 360c(f)(2)(A); 21 C.F.R. subpart D (2024).

can obtain FDA approval based on data using surrogate endpoints instead of the clinical benefit required under traditional approval.[166] Because these cases have not yet been litigated, this Article does not analyze them directly.[167] Its analysis of off-label promotion claims, however, applies equally to these pathways to market.

C. Off-Label Preemption

Claims that manufacturers should be liable under state law for promoting their drugs and devices off-label must also confront the preemption question.[168] Devices implicate both express (for PMA devices) and implied preemption (for 510(k) devices) while drugs implicate only the latter. This Section explores each sequentially.

1. DEVICES: EXPRESS AND IMPLIED PREEMPTION

Federal law expressly preempts state law claims against drug and device manufacturers based on off-label promotion only when there exists (1) a federal requirement applicable to the device, and (2) a state law requirement applicable to the device that is different from or in addition to the federal one.[169] Federal law impliedly preempts state law claims premised solely on a violation of federal law.

Every court to consider the first issue has concluded that the "federal requirements" applicable to PMA devices do not change when a device is used off-label.[170] The "only logical reading" of Section 360k, they

166. 21 U.S.C. § 356(c); 21 C.F.R. § 314.510.

167. For an analysis of this issue, see David A. Simon, Carmel Shachar & I. Glenn Cohen, *Innovating Preemption or Preempting Innovation?*, Nw. U. L. REV. ONLINE (forthcoming 2024) (on file with author).

168. In the device context, there is at least one recent case where preemption was not raised. *Shahbaz v. Johnson & Johnson*, No. 13-cv-07382, 2020 WL 5894590, at *8–11 (C.D. Cal. July 31, 2020) (denying summary judgment for off-label use claim without discussing preemption). The case settled two years after the court allowed some claims to proceed. Order Dismissing Civil Action, *Shahbaz*, No. 13-cv-07382 (C.D. Cal. Feb. 14, 2022), https://docs.justia.com/cases/federal/district-courts/california/cacdce/2:2013cv07382/573491/65.

169. As noted above, this federal requirement must relate to the safety and effectiveness of the device. *See supra* notes 108–10 and accompanying text. Again, however, discussion of this component is left out because it is rarely implicated.

170. *E.g.*, *Cales v. Baptist Healthcare Sys., Inc.*, No. 2015-CA-001103, 2017 WL 127731 (Ky. Ct. App. Jan. 13, 2017); *Angeles v. Medtronic, Inc.*, 863 N.W.2d 404 (Minn. Ct. App. 2015); *Bertini v. Smith & Nephew, Inc.*, 8 F. Supp. 3d 246 (E.D.N.Y. 2014); *Gavin v. Medtronic, Inc.*, No. 12-0851, 2013 WL 3791612, at *11 (E.D. La. July 19, 2013); *Schouest v. Medtronic, Inc.*, 13 F. Supp. 3d 692, 703–04 (S.D. Tex. 2014). Most courts take this as a given. *See e.g.*, *Arthur v. Medtronic, Inc.*, No. 14-CV-52, 2014 WL 3894365, at *4 (E.D. Mo. 2014) ("There is no dispute that the Infuse device

claim, is that PMA requirements "appl[y] to the device," not the uses of the device.[171] Some justify this decision by pointing to the statutory text and the most recent Supreme Court case examining the issue (*Riegel v. Medtronic, Inc.*[172]), both of which referred to devices, not uses of devices.[173] Others assume that a contrary holding would violate FDA's statutory duty to refrain from regulating the practice of medicine,[174] with one court stating that this "illegitimately shifts the risk of off-label use from prescribing doctors and patients to manufacturers."[175] The same holding generally applies when a 510(k)-cleared component of a PMA device is promoted and used off-label,[176] typically justified by the same rationale.[177]

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obtained premarket approval and thus the first prong of the Riegel analysis is satisfied."); *Wolicki-Gables v. Arrow Int'l, Inc.*, 634 F.3d 1296, 1300–02 (11th Cir. 2011). Ironically, the most forceful rejection of the off-label distinction is the one that overlooks the key definition in the statute. *Caplinger v. Medtronic, Inc.*, 784 F.3d 1335, 1344–47 (10th Cir. 2015).

171. *See, e.g.*, *Cales*, 2017 WL 127731, at *10.

172. 552 U.S. 312 (2008).

173. *E.g.*, *Riley v. Cordis Corp.*, 625 F. Supp. 2d 769, 778–79 (D. Minn. 2009) ("Even assuming that *Riegel* does not foreclose the argument that off-label use renders § 360k(a) inapplicable, that argument must fail because it is inconsistent with the text of the statute. . . . [U]nder § 360k(a)(1), the question is not whether there are federal requirements applicable to a particular *use* of a device; the question is whether there are federal requirements applicable 'to the *device*.'"); *Brady v. Medtronic, Inc.*, No. 13-cv-62199, 2014 WL 1377830, at *5 (S.D. Fla. 2014) ("The language of § 360k(a) is extremely broad. There is nothing in the provision that suggests that the applicability of the preemption analysis turns on either how the device was used or marketed, or on the conduct of the manufacturer.").

174. *Angeles*, 863 N.W.2d at 411.

175. *Clements v. Sanofi-Aventis, U.S., Inc.*, 111 F. Supp. 3d 586, 601 (D.N.J. 2015) (citing *Caplinger*, 784 F.3d 1335, favorably). *See also Garross v. Medtronic, Inc.*, 77 F. Supp. 3d 809, 814–15 (E.D. Wis. 2015).

176. *E.g.*, *Shuker v. Smith & Nephew, PLC*, 885 F.3d 760, 773 (3d Cir. 2018); *Arvizu v. Medtronic Inc.*, 41 F. Supp. 3d 783, 790 (D. Ariz. 2014); *Martin v. Medtronic, Inc.*, 32 F. Supp. 3d 1026, 1034–36 (D. Ariz. 2014); *Beavers-Gabriel v. Medtronic, Inc.*, 15 F. Supp. 3d 1021, 1032–33 (D. Haw. 2014); *Scovil v. Medtronic, Inc.*, 995 F. Supp. 2d 1082, 1095 (D. Ariz. 2014); *Houston v. Medtronic, Inc.*, No. 13-cv-10679, 2014 WL 1364455, at *4 (C.D. Cal. Apr. 2, 2014); *Gavin v. Medtronic, Inc.*, No. 12-0851, 2013 WL 3791612, at *11–12 (E.D. La. July 19, 2013) (citing favorably *Bass v. Stryker Corp*, 669 F.3d 501 (5th Cir. 2012)). *But see Hornbeck v. Medtronic, Inc.*, No. 13 C 7816, 2014 WL 2510817, at *4 (N.D. Ill. June 2, 2014) (asserting that claims as to off-label component use are not expressly preempted); *Ramirez v. Medtronic Inc.*, 961 F. Supp. 2d 977, 990–93 (D. Ariz. Aug. 21), *clarified on denial of reconsideration* (D. Ariz. Oct. 24, 2013); *Caplinger v. Medtronic, Inc.*, 784 F.3d 1335, 1348–50 (10th Cir. 2015) (Lucero, J., concurring in part and dissenting in part) (noting that this reasoning would grant immunity to device manufacturers from injuries resulting from misbranding or adulteration practice).

177. *E.g.*, *Shuker*, 885 F.3d at 772–73.

Courts have slightly diversified their approaches on the second express preemption issue. Some conclude that state law claims based on off-label use or off-label promotion impose requirements "different from, or in addition to" the federal ones.[178] They reason that FDA reviews risks and mandates particular disclosures, but not for off-label promotion.[179] Imposing state law duties to warn of off-label risks or provide additional instructions would add to the existing federal requirements,[180] though in some cases fraudulent representation claims may survive.[181] Design defect claims, predictably, suffer from the same problem: they would require manufacturers to make a different device from the one FDA approved.[182]

Others disagree, noting that some or all state law claims based on off-label promotion parallel federal requirements.[183] Of these courts, some clearly state that off-label promotion violates federal law[184] and

178. *E.g.*, *Byrnes v. Small*, 60 F. Supp. 3d 1289, 1297 (M.D. Fla. 2015) ("Accordingly, regardless of whether Medtronic engaged in off-label promotion of Infuse, such requirements would clearly be different from, or in addition to, the federal requirements.").

179. *Dawson v. Medtronic, Inc.*, No. 13-cv-663, 2013 WL 4048850, at *4–7 (D.S.C. Aug. 9, 2013); *Norabuena v. Medtronic, Inc.*, 86 N.E.3d 1198, 1207–08 (Ill. App. Ct. 2017).

180. *Hafer v. Medtronic, Inc.*, 99 F. Supp. 3d 844, 856, 860, 862–63 (W.D. Tenn. 2015); *Coleman v. Medtronic, Inc.*, 167 Cal. Rptr. 3d 300, 312–14 (Ct. App. 2014); *Scanlon v. Medtronic Sofamor Danek USA Inc.*, 61 F. Supp. 3d 403, 411–12 (D. Del. 2014); *Schouest v. Medtronic, Inc.*, 13 F. Supp. 3d 692, 703–04 (S.D. Tex. 2014); *Stengel v. Medtronic Inc.*, 704 F.3d 1224, 1234 (9th Cir. 2013) (Watford, J., concurring) ("Where a federal requirement permits a course of conduct and the state makes it obligatory, the state's requirement is in addition to the federal requirement and thus is preempted." (quoting *McMullen v. Medtronic, Inc.*, 421 F.3d 482, 489 (7th Cir. 2005))); *Dawson*, 2013 WL 4048850, at *7; *Byrnes v. Small*, 142 F. Supp. 3d 1262, 1272 (M.D. Fla. 2015); *Riley v. Cordis Corp.*, 625 F. Supp. 2d 769, 783 (D. Minn. 2009) (holding unilateral change to label possible but a state law requirement that made this mandatory would be an additional or different requirement from the federal one).

181. *E.g.*, *Schouest*, 13 F. Supp. 3d at 704.

182. *See, e.g.*, *Wright v. Medtronic, Inc.*, 81 F. Supp. 3d 600, 613 (W.D. Mich. 2015); *Jones v. Medtronic*, 89 F. Supp. 3d 1035, 1052 (D. Ariz. 2015) (dismissing design defect claims as expressly preempted), *aff'd in part, vacated in part*, 745 F. App'x 714 (9th Cir. Aug. 16), *amended on denial of reh'g* (9th Cir. Sept. 7, 2018) (affirming holding design defect preempted).

183. *E.g.*, *Hafer*, 99 F. Supp. 3d at 859, 861–62; *Arvizu v. Medtronic Inc.*, 41 F. Supp. 3d 783, 790–92 (D. Ariz. 2014) (fraud claims based on off-label promotion parallel but failure to warn claims expressly preempted based on *Stengel* because physician warnings would be different from or in addition to what FDA requires).

184. *Ramirez v. Medtronic Inc.*, 961 F. Supp. 2d 977, 986 (D. Ariz.) (noting that "[a] manufacturer is . . . prohibited from promoting a use of the product that is not the specified use" and citing to 21 C.F.R. § 814.80, which prohibits labeling or advertising with "any conditions to approval specified in the PMA approval order for the device"), *clarified on denial of reconsideration* (Oct. 24, 2013); *Garross v. Medtronic,*

state law claims like negligence, fraud, and even design defect claims parallel them too.[185] Of those that find federal and state law duties run parallel, some say that FDA regulations requiring the manufacturer to report certain adverse events[186] parallel to duty to warn claims,[187] or conclude only that fraud claims are true parallel claims, presumably because false and misleading statements are prohibited by federal law.[188]

Inc., 77 F. Supp. 3d 809, 815 (E.D. Wis. 2015); *Riley*, 625 F. Supp. 2d at 783 (noting that during the relevant period FDA regulations allowed certain kinds of off-label promotion and if violated could form a parallel claim but it would be impliedly preempted); *Carson v. Depuy Spine, Inc.*, 365 F. App'x 812, *815 (9th Cir. 2010) ("[T]he marketing and promotion of a Class III device for an unapproved use violates Section 331 of the FDCA."). *See also* 21 C.F.R. § 814.80 (2023) ("A device may not be manufactured, packaged, stored, labeled, distributed, or advertised in a manner that is inconsistent with any conditions . . . specified in the PMA approval order for the device.").

185. *Garross*, 77 F. Supp. 3d at 815 ("Class III medical device manufacturers are required to report adverse events to the FDA, 21 C.F.R. § 803.50, investigate serious adverse events and submit follow-up reports, 21 C.F.R. § 803.56, and submit a supplemental application for approval of additional uses of a medical device. 21 C.F.R. § 814.39 (listing 'new indications for use of the device' as a change requiring supplemental FDA approval)."); *id.* at 816. *But see Hafer*, 99 F. Supp. 3d 844.

186. On reporting "serious injury," see 21 U.S.C. §§ 360i(a)(1)–(2); 21 C.F.R. § 803.3(a)(2), .50(a).

187. *Hughes v. Bos. Sci. Corp.*, 631 F.3d 762, 770–71 (5th Cir. 2011); *Stengel v. Medtronic Inc.*, 704 F.3d 1224, 1233–34 (9th Cir. 2013); *Garross*, 77 F. Supp. 3d at 814–16 (noting that "Class III medical device manufacturers are required to report adverse events to the FDA" under 21 C.F.R. § 803.50, "investigate serious adverse events and submit follow-up reports" under 21 C.F.R. § 803.56, and "submit a supplemental application for approval of additional uses of a medical device" under 21 C.F.R. § 814.39, which "list[s] 'new indications for use of the device' as a change requiring supplemental FDA approval" (quoting 21 C.F.R. § 814.39)); *Jones*, 745 F. App'x at *717 (allowing amendment for claims based on failure to report adverse events to FDA, which caused FDA not to issue warnings, which caused plaintiff's injuries, because such claims would not be expressly preempted, and allowing the same with respect to failure to update labeling for a new use based on 21 C.F.R. § 801.4); *Schouest v. Medtronic, Inc.*, 13 F. Supp. 3d 692, 706 (S.D. Tex. 2014). *But see, e.g.*, *Tillet v. CooperSurgical, Inc.*, 23-cv-06031, 2023 WL 4704091, at *4 (W.D.N.Y. July 24, 2023) (holding adverse event reporting not parallel to state law duty in on-label context because warning may not reach physician). Other courts note that even if the claims survive express preemption, they may be impliedly preempted.

188. *Schouest*, 13 F. Supp. 3d at 704; *Zaccarello v. Medtronic, Inc.*, 38 F. Supp. 3d 1061, 1070–71 (W.D. Mo. 2014) (holding that fraud claim is parallel and survives preemption, but that it fails on pleading). *See also Riley*, 625 F. Supp. 2d at 781 (finding violation of federal law on the face of now-sunset provisions of FDCA and its implementing regulations). *But see Jones*, 745 F. App'x at *717 (holding fraud claim failed because plaintiff had not alleged that *she* relied on fraudulent statements); *Frere v. Medtronic, Inc.*, No. EDCV 15-02338, 2016 WL 1533524, at *9–10 (C.D. Cal. Apr. 6, 2016) (fraud claim preempted because it is effectively a fraud-on-FDA claim). As noted in Part I, these are not the only kinds of statements prohibited by federal law and prosecuted by FDA.

Claims against device manufacturers based on off-label promotion may also be impliedly preempted. Preemption applies if a plaintiff alleges *merely* that FDA should not have approved a drug, for instance, because the information defendant relied on in approving the drug or device was fraudulent.[189] Claims premised on failure to report adverse events, mentioned above, may not be preempted.[190] When off-label promotion cases involve PMA-devices, this implied preemption can get mixed in with express preemption's second prong.[191]

All this speaks to the broader issue of whether the plaintiff's claim identifies a state law duty that "predate[s] the federal enactments."[192] This, it turns out, is the fundamental issue for both drugs and devices facing implied preemption defenses: Is there an independent state law duty on which to rest off-label promotion claims? For devices, there are two views. One holds there is no independent state law duty not to engage in off-label promotion. Claims based on off-label promotion, then, are impliedly preempted—they are essentially fraud-on-the-FDA claims.[193] Another finds that while off-label promotion is not prohibited under state law, tort, contract, and state law claims are "genuinely equivalent" to the prohibitions on off-label promotion, misbranding, or adulteration.[194]

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189. *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 352, 347–53 (2001).

190. *Hughes*, 631 F.3d at 775–76; *Stengel*, 704 F.3d at 1233. *See also Bass v. Stryker Corp.*, 669 F.3d 501, 516–17 (5th Cir. 2012) (finding implied warranty claim neither expressly nor impliedly preempted).

191. *E.g.*, *Scovil v. Medtronic, Inc.*, 995 F. Supp. 2d 1082, 1096 (D. Ariz. 2014) ("However, the Court finds that Plaintiffs' allegations concerning the marketing of the device (alternatively labeled 'merchandising,' 'advertising,' and 'promoting') are not preempted. Plaintiffs allege that Defendants engage in off-label promotion, which violates federal law. *See* 21 C.F.R. §814.80; *Carson*, 365 Fed. Appx. at 815. Yet they are not suing merely because such conduct violated federal law, but rather because it violated pre-existing state common law of negligence. Thus, the Court finds that Count Four fits in the 'narrow gap' of state law claims that are not preempted. *See Perez*, 711 F.3d at 1120.")

192. *Buckman*, 531 U.S. at 353.

193. *See, e.g.*, *Zaccarello*, 38 F. Supp. 3d at 1068; *Blankenship v. Medtronic, Inc.*, 6 F. Supp. 3d 979, 987, 989–91 (E.D. Mo. 2014) (distinguishing *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012), as a criminal case but reaching the same conclusion); *Houston v. Medtronic, Inc.*, 957 F. Supp. 2d 1166, 1178 (C.D. Cal. 2013); *Byrnes v. Small*, 60 F. Supp. 3d 1289, 1297 (M.D. Fla. 2015) (claim based on adverse event reporting impliedly preempted). *See also Perez v. Nidek Co.*, 711 F.3d 1109, 1118–19 (9th Cir. 2013) (finding fraud claim preempted based on failure of physicians to disclose off-label use to patients).

194. *Ramirez v. Medtronic Inc.*, 961 F. Supp. 2d 977, 994–96 (D. Ariz. Aug. 21), *clarified on denial of reconsideration* (D. Ariz. Oct. 24, 2013). *See also, e.g.*, *Eidson v. Medtronic, Inc.*, 40 F. Supp. 3d 1202, 1227–28 (N.D. Cal. 2014) (distinguishing *Perez* as a straight omission case and holding "that California common law unquestionably prohibits commercial misrepresentations and omissions such as those

Sometimes courts reach opposite conclusions on different claims in the same opinion,[195] or across jurisdictions.[196]

2. DRUGS: IMPLIED PREEMPTION

These two views are mirrored in the drug context. One view is that any federal law prohibiting promotion impliedly preempts state law claims because the latter exist only by virtue of the former.[197] The other is that preemption does not apply because the violation of federal law is not the sole basis for the claim; the act of off-label promotion includes the prohibited state law conduct.[198] Sometimes what distinguishes these two views is what the plaintiff alleged.[199] Without allegations of some underlying state law duty, such as fraud,[200] courts will dismiss the

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alleged here, . . . and thus Plaintiffs' state law claims predate and arise independently of the federal regulations and do not exist solely by virtue of the FDCA." (citation omitted)).

195. *E.g.*, *Byrnes*, 60 F. Supp. 3d at 1297–300.

196. *Compare id.* at 1297 (finding the claim based on a failure to warn either expressly or impliedly preempted), *with Stengel v. Medtronic Inc.*, 704 F.3d 1224, 1233 (9th Cir. 2013) (holding that a claim of failure to report adverse events to FDA is not expressly or impliedly preempted).

197. *See, e.g.*, *Frei v. Taro Pharms. U.S.A., Inc.*, 443 F. Supp. 3d 456, 468–69 (S.D.N.Y. 2020); *Bean v. Usher-Smith Pharms., Inc.*, No. 16-cv-01696, 2017 WL 4348330, at *7 (D.S.C. Sept. 29, 2017), *aff'd*, 765 F. App'x. 934 (4th Cir. 2019); *McLeod v. Sandoz, Inc.*, No. 16-cv-01640, 2017 WL 1196801, at *4–7 (D.S.C. Mar. 31, 2017) (finding the negligence and failure to warn claims preempted, under *Mensing* and *Bartlett*, but fraud claim not impliedly preempted); *Perdue v. Wyeth Pharms., Inc.*, 209 F. Supp. 3d 847, 852 (E.D.N.C. 2016) (holding that plaintiff failed to identify any state law duty predating FDCA that prohibits off-label promotion); *Simpkins v. Grandview Hosp.*, No. 19-cv-227, 2020 WL 4220460, at *9 (S.D. Ohio July 23) (recommending that the claim of off-label use is preempted because alleged only that promoted off-label), *report and recommendation adopted in part*, *rejected in part*, No. 19-cv-227, 2020 WL 5362054 (S.D. Ohio Sept. 8, 2020) (accepting magistrate judge's report and recommendation on preemption).

198. *Knipe v. SmithKline Beecham*, 583 F. Supp. 2d 602, 619–35 (E.D. Pa. 2008) (deciding, before *Wyeth*, no preemption of claims based on off-label promotion because conduct involved fraud to physicians after marketing). *See also Rosenstern v. Allergan, Inc.*, 987 F. Supp. 2d 795, 804 (N.D. Ill. 2013) (noting that design defect claim based on off-label use not preempted at motion to dismiss stage but could be preempted later). In the insurer context, see *Aetna Inc. v. Insys Therapeutics, Inc.*, 324 F. Supp. 3d 541, 555 (E.D. Pa. 2018).

199. *Markland v. Insys Therapeutics, Inc.*, 758 F. App'x 777, *780 (11th Cir. 2018) (finding the claim was preempted because of the plaintiff's failure to allege state law duty, and off-label is a concept created by federal statute).

200. Fraud is frequently singled out among courts as a plausible state law duty, but it is also frequently dismissed for failure to plead with particularity. *E.g.*, *Tutwiler v. Sandoz Inc.*, No. 16-cv-01246, 2017 WL 11609669, at *4 (N.D. Ala. Mar. 9, 2017); *Elliott v. Sandoz, Inc.*, No. 16-cv-00861, 2016 WL 4398407, at *7–9 (N.D. Ala. Aug. 18, 2016).

plaintiff's claims.[201] Other times the distinction is clearer—with some courts defining the state law claim in terms of "off-label promotion"[202] (preempted) and others defining the conduct that state law covers (not preempted).[203]

Despite these difficulties, marketing defect claims relating to certain *types* of off-label uses may be easier to slip through *Wyeth* and *Buckman* than others.[204] That is because FDA actually requires warnings about some off-label uses—pediatric,[205] geriatric,[206] and labor and delivery[207]—to appear on the label, though it says nothing about voluntary changes.[208] By reading the CBE regulations to apply to these "off-label, on-label" uses, some courts have allowed marketing defect claims to proceed against manufacturers under *Wyeth* on the traditional theory: they failed to update labels with the specific information about these off-label uses.[209]

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201. *See Kelley v. Insys Therapeutics, Inc.*, No. 18CV1774, 2019 WL 329600, at *3 (N.D. Ohio Jan. 25, 2019) ("Although some of plaintiffs' claims are solely for off-label promotion and are preempted, independent state-law grounds support others, which survive plaintiffs' motion to dismiss.").

202. *Markland*, 758 F. App'x at *780 (holding Markland failed to allege a state law duty because "off-label" is a concept created by federal statute).

203. *Arters v. Sandoz Inc.*, 921 F. Supp. 2d 813, 820 (S.D. Ohio 2013) (holding that, prior to *Bartlett* and concerning a generic drug, off-label promotion claim was grounded in state law); *In re Nat'l Prescription Opiate Litig.*, No. 17-cv-02804, 2018 WL 4895856, at *26 (N.D. Ohio Oct. 5), *report and recommendation adopted in part, rejected in part*, No. 17-cv-02804, 2018 WL 6628898 (N.D. Ohio Dec. 19, 2018) ("Plaintiffs do not seek to enforce the provisions of the FDCA, instead they allege that Defendants fraudulently and misleadingly promoted their opioids."); *In re Testosterone Replacement Therapy Prods. Liab. Litig.*, No. 14 C 1748, 2017 WL 1836443, at *7 (N.D. Ill. May 8, 2017) (finding that off-label promotion claims were not preempted "because the claims are grounded in traditional state law principles of liability, such as negligence, failure to warn, strict product liability, and fraud that predate the relevant FDCA requirements").

204. For true off-label uses (*i.e.*, those that are not required on the label), FDA regulations also require manufacturers to update labels to account for off-label uses with "a clinically significant risk or hazard." *See* 21 C.F.R. §§ 201.57(c)(6), .80(e) (2024). At least one court has held the failure to warn theories based on these risks are not impliedly preempted *even in the absence of promoting the off-label use*. *Wendell v. SmithKline Beecham*, No. 09-04124, 2018 WL 6267855, at *7 (N.D. Cal. Aug. 15, 2018).

205. 21 C.F.R. §§ 201.57(c)(9)(iv)(E)–(F), .80(f)(9)(v)–(vi).

206. 21 C.F.R. §§ 201.57(c)(9)(v)(D), .80(f)(10)(iv).

207. 21 C.F.R. §§ 201.57(c)(9)(i)(C)(5), .80(f)(7) (requiring description of expected effects of any off-label use).

208. It is plausible to read the CBE exception to allow voluntary changes to the labeling to reflect otherwise required information about off-label uses.

209. *A.Y. v. Janssen Pharms. Inc.*, 224 A.3d 1, 15 (Pa. Super. Ct. 2019) (holding that under a previous version of the relevant regulations governing the use at issue (21 C.F.R. § 201.57(f)(9)(i) (2003)), drug labeling had to include "specific hazards" associated with an unapproved pediatric use and drawing on *Wyeth* and the CBE

Generic drugs are swept up by the *Bartlett* and *Mensing* rulings, with courts generally holding that generic manufacturers have no duty to warn or mitigate the statements of brand name manufacturers based on off-label promotion by a brand manufacturer.[210] But at least two courts, following the second view just discussed, have suggested that *Bartlett* and *Mensing* do not foreclose claims based on off-label promotion.[211]

exception for support). *See also Simon v. Wyeth Pharms., Inc.*, 989 A.2d 356, 368–76 (Pa. Super. Ct. 2009) (reversing a judgment notwithstanding the verdict and affirming the jury verdict on a failure to warn claim under the learned intermediary doctrine premised on inadequate warnings during off-label promotion but discussing only the issue of causation).

210. *See, e.g.*, *Jankowski v. Zydus Pharms. USA, Inc.*, No. 22-2212, 2023 WL 4700651 (3d Cir. July 24, 2023); *Frei v. Taro Pharms. U.S.A., Inc.*, 443 F. Supp. 3d 456, 468–69 (S.D.N.Y. 2020); *Kellogg v. Wyeth*, No. 07-cv-82, 2012 WL 368658, at *5 (D. Vt. Feb. 3, 2012) (holding that *Mensing* bars all claims, regardless of promotion on- or off- label); *Bean v. Upsher-Smith Pharms., Inc.*, No. 16-CV-01696, 2017 WL 4348330, at *5 (D.S.C. Sept. 29, 2017), (holding that off-label promotion claims are preempted by *Mensing* and *Bartlett*), *aff'd*, 765 F. App'x 934 (4th Cir. 2019) (preemption claims not appealed); *LeBoeuf v. Janssen Pharms., Inc.*, No. CV 16-12419, 2017 WL 175781, at *2 (E.D. La. Jan. 17, 2017) (finding the claims based on off-label use preempted under *Mensing*); *Tutwiler v. Sandoz Inc.*, No. 16-cv-01246, 2017 WL 11609669, at *3 (N.D. Ala. Mar. 9, 2017) (dismissing failure to warn claim against generic manufacturer based on not distributing medication guide as preempted based on *Mensing* and the learned intermediary doctrine); *Connolly v. Sandoz Pharms. Corp.*, No. 14-CV-152, 2014 WL 12480025 (N.D. Ga. Dec. 23, 2014).

211. *Lempa v. Eon Labs, Inc.*, No. 18 C 3821, 2019 WL 1426011, at *4 (N.D. Ill. Mar. 29, 2019) (holding the state law claims do not depend on federal law and are not preempted); *Tutwiler*, 2017 WL 11609669, at *4 (construing off-label promotion claims as fraud claims against the brand manufacturer with benefits that redound to the defendant generic manufacturer, finding them not preempted but insufficiently pled because she failed to identify any statements made by the *generic* manufacturer).

On- or Off-Label	Brand or Generic	Claim Type Preempted		
		Manufacturing	*Design*	*Warning*
On-Label	Brand	No	Yes	Some
Off-Label	Brand	No	Yes	Maybe
On-Label	Generic	No	Yes	Yes
Off-Label	Generic	No	Probably Yes	Probably Yes

Table 5. Preemption of Claims against Prescription Drug Manufacturers by Claim Type.

3. SUMMARY

Preemption in the off-label context is at least as confusing as in the on-label context. Courts seem to almost uniformly agree that off-label promotion does not change how express preemption applies to devices in the first instance. That is, they agree that federal requirements applicable to PMA devices also apply regardless of whether the manufacturer promoted an off-label use of its product. They are divided, however, on whether state law claims based on off-label promotion are parallel. Implied preemption analysis for drugs and devices exhibits a similar split, with some courts holding that state law claims based on off-label promotion are preempted as fraud-on-the-FDA claims and others holding that they are not preempted because they are grounded in an independent state law duty that precedes the MDA.

III. AN APPROVAL THEORY OF OFF-LABEL PREEMPTION

This Article has shown that courts applied conflict preemption differently depending on the statutory language (express or implied), the product (drug or device), and the use (on- or off-label). This Part proposes an approval theory that explains why preemption should not apply to state law claims based on off-label promotion. Section III.A explains this theory and how it fits within the preemption doctrine's broader theoretical framework. Section III.B explains why this theory comports with and is supported by Supreme Court precedent, highlighting the doctrinal mistakes lower courts have made when

deciding preemption cases involving off-label promotion. Section III.C explains the policy reasons that support the approval theory.

A. An Approval Theory of Off-Label Preemption

Under the approval theory, the doctrine of preemption applies only when the risks involved have been reviewed by FDA *as to approved uses*. When FDA has not yet reviewed a risk or has reviewed a risk associated with a use it has not approved, preemption should not apply. Since most off-label risks may not be reviewed by FDA nor expected to be part of risk-benefit calculus as to the approved use, federal law should not preempt state law claims based on off-label promotion.

This approach is consistent with the purpose of preemption, which, in the drug and device context, exists to prevent conflicts between federal and state regulation, not to supplant the entire field of state law. With respect to the labeling and design of drugs and devices, federal law regulates risk ex ante through FDA's review. To reach the market, for example, drug and device manufacturers must pass through FDA review and conform to FDA regulations, including those regarding labeling. Preemption is meant to govern conflicts that arise with respect to this regulation of risk.

Conflict arises, and preemption applies, when state law substitutes FDA's judgment on a particular risk FDA has considered as to an approved use. For example, a state can disrupt the regulatory scheme by enacting a law mandating design for drugs or devices that differs from federal law. For example, a state may mandate that drugs must undergo supplemental testing under state law before marketing in that state. Here, FDA has made a determination about the kind of risk it will tolerate and mandated labeling required to mitigate it. If state law requires testing and subsequent labeling that is stricter than federal law, the manufacturer cannot comply with state law without violating federal law. Even if it is possible to comply, allowing states to set risk standards through positive law would undermine one purpose of federal regulation: the unification under one federal umbrella the diverse array of state laws regarding "pure food and drugs."[212]

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212. *See Pure Food and Drugs*, NAT'L INST. MED.: HIST. MED., https://www.nlm.nih.gov/exhibition/phs_history/foodanddrugs.html [https://perma.cc/UB9J-43T8]. For a discussion of this issue over time and in historical context, see, for example, George M. Burditt, *The Importance of Uniformity Among State Food and Drug Laws*, 25 BUS. LAW. 1749 (1970); George M. Burditt, *Uniformity—A Legislator's Viewpoint*, 21 FOOD DRUG COSM. L.J. 145 (1966); William W. Goodrich, *Uniformity in Federal-State Food Regulations*, 17 FOOD DRUG COSM. L.J. 305 (1962); Ole Salthe, *State Food, Drug and Cosmetic Legislation and Its Administration*, 6 LAW & CONTEMP. PROBS. 165 (1939).

Not all state laws, however, conflict with federal ones. And without a conflict, federal law does not preempt state law claims.[213] When FDA does not review a particular risk, then state law regulating that risk will not conflict with federal law. But, and this is a critical point, *even when FDA has reviewed a particular off-label use*, its review of associated risks may not have been comprehensive or sufficient to form a basis for an opinion on those risks. Indeed, the opposite may be true: if FDA considered a proposed use that it did not approve, it may have concluded the benefit of the use did not outweigh the risk—meaning the use, or the risks associated with it, should not appear on the labeling.

And this leads to another, perhaps more important point about these off-label risks: the notice function served by FDA approval may be missing. States, physicians, and patients cannot know about risks FDA may have considered for an unapproved use that never makes it on the label. For one thing, since the use is unapproved, it is not clear whether FDA considered it. For another, if FDA did consider some off-label risks, it is impossible for physicians and consumers to know which ones or what FDA thought about them.[214] All of this underscores a fundamental problem for FDA and consumers who rely on it: risks associated with off-label risks are at best uncertain and at worst unknowable.

In these cases, too, applying preemption to bar claims is inappropriate since FDA has not necessarily made a determination as to the significance of a particular *labeled* use, and it may have made negative determinations about the off-label use and its attendant risks. State law requiring disclosure of the risks associated with off-label uses preserves the notice function that approval and labeling decisions normally serve without conflicting with state law.

State law claims based on off-label promotion avoid conflict, then, because FDA has not yet reviewed off-label risks comprehensively or because their review of a particular risk has not been, or cannot be, officially communicated to physicians through an approval decision. This is different from the on-label context where FDA's approval and labeling communicates risk information to physicians: approval decisions to include particular risks on the label necessarily include determinations about which risks not to include. In the off-label context, by contrast, FDA does not include information about many off-label risks because the

213. Absent field preemption, of course.

214. The fact that FDA may consider off-label use as part of its risk-benefit analysis does not alter this analysis. FDA is not in a position to evaluate all potential uses or risks associated with them. And even this risk calculation is for *the on-label use*. That is, the FDA asks whether the on-label use is worth the potential risk posed by some (unidentified) off-label uses that may occur.

off-label use is not approved. As a result, physicians in the off-label context do not have the same type of notice, even for risks FDA may have considered, as they do in the on-label context.

Consider the example of the Infuse Bone Graft discussed in the Introduction. Because Medtronic's approval was confined to uses of the device in certain parts of the lower spine, FDA did not evaluate off-label uses in other parts of the spine. It was aware, however, that the device could have potential negative consequences if used off-label.[215] Yet it could not evaluate the off-label use comprehensively because it did not have the data to do so. An FDA Advisory Committee panel even expressed specific concerns about how Medtronic would guard against off-label use.[216] But those concerns are not sufficiently expressed in or communicated by its approval vis-à-vis physicians. Although the label made the standard passing reference to the lack of safety and effectiveness evaluation for off-label uses and bone growth in the lower spine, it did not communicate to physicians the scope and scale of potential risks involved in promoted off-label uses.[217] Applying preemption here makes little sense because FDA could not fully consider the risks and its approved labeling did not communicate them sufficiently. The approval theory, in other words, would prevent Medtronic from successfully asserting the defense of preemption.

Concerns that typically drive preemption forward here counsel in favor of its retreat. We do not have to worry that "the MDA was meant to 'grant greater power . . . to a single state jury than to state officials acting through state administrative or legislative lawmaking processes'"[218] because FDA has not yet evaluated off-label uses prior to marketing.[219] Or, if it has, FDA has found those uses not to warrant approval. Yet this information has not been communicated through an affirmative approval decision in the same way—lack of approval does not necessarily signify that FDA has evaluated any or all off-label risks in

215. InFuse Bone Graft Approval Letter, *supra* note 1, at 2 (requesting post-approval studies to assess the device in part "[b]ecause of the unknown long-term device performance, particularly the resulting bony fusion characteristics").'

216. This meeting transcript is not available online. The information comes from Complaint for Damages at 17–18, *Ramirez v. Medtronic Inc.*, 961 F. Supp. 2d 977, 995–96 (D. Ariz. Aug. 21), *clarified on denial of reconsideration* (D. Ariz. Oct. 24, 2013).

217. INFUSE™ BONE GRAFT/LT-CAGE™ LUMBAR TAPERED FUSION DEVICE IMPORTANT MEDICAL INFORMATION 3 (2002), https://www.accessdata.fda.gov/cdrh_docs/pdf/P000058C.pdf.

218. *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 325 (2008) (quoting *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 504 (1996)).

219. In certain circumstances, FDA may also require additional warnings regarding off-label risks. *See supra* notes 204–07 and accompanying text.

the same manner as those related to on-label uses. Off-label risks can remain within the knowledge of the manufacturer and FDA unknown (or obscured) to physicians to whom the uses are promoted.

Here state law provides an additional incentive to disclose risks when promoting off-label uses. Under either the strong (off-label use is illegal) or weak (off-label use is not a requirement) version of this argument, the effect is the same. Juries are asked to do something federal officials are not: evaluate whether an off-label promotion failed to warn, misrepresented, or rendered a design defective.

Nor will state law claims based on off-label promotion cause applicants to "submit a deluge of information that the Administration neither wants nor needs, resulting in additional burdens on the FDA's evaluation of an application."[220] Applicants that wish to promote off-label uses have nothing additional to submit to FDA. And because prospective off-label uses are not part of the manufacturer's *approved* application, state law liability will not have any effect on application content.[221]

To the contrary, the approval theory is consistent with the Supreme Court's repeated reaffirmations that "state rights of action provide[] appropriate relief for injured consumers" and "further consumer protection by motivating manufacturers to produce safe and effective drugs and to give adequate warnings."[222] The theory neatly and cleanly sweeps away the morass of distinctions judges have erected in trying to decide claims based on off-label promotion. Because FDA has not yet evaluated many off-label risks, federal law does not preempt state law claims based on off-label promotion, making the tortious doctrinal analysis unnecessary.

Before moving on, however, there is one final issue that is left unresolved by the discussion before: should preemption apply to *all* off-label risks or simply those *new or altered* risks posed by the off-label use? While the former are clearly not preempted under the approval theory, the latter may be. If the labeled risk of a drug is suicidality, for example, then it *may* be reasonable, depending on the use, for physicians to expect that an off-label use may also have that same risk. Thus, where risk information that appears on the drug label is *equally applicable* to the off-label use at issue, the manufacturer may properly assert preemption as a defense.

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220. *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 351 (2001).

221. One or more of an applicant's proposed on-label uses may ultimately become off-label uses if FDA narrows or rejects them. Even if FDA has data on what become off-label uses, however, it approves a drug for a particular use, not for an off-label use. The fact that an off-label use was not approved suggests it should not be promoted without consequence.

222. *Wyeth v. Levine*, 555 U.S. 555, 574 (2009).

But this should not necessarily result in a judgment against the plaintiff for two reasons. First, the nature of the risk's applicability may be disputed (scientifically). A risk of suicidality for an on-label use, for example, may seem to apply equally to an off-label use. But if the dosage, route of administration, or patient population is different, it may not. The risk may be much higher for the off-label use than the on-label use. Second, the nature of the defendant's communication may affect the applicability analysis since it is not about the labeled use. How the manufacturer communicates the off-label use and attendant risks can influence its disclosure of the on-label one, even through labeling. Excessive off-label promotion may even vitiate the labeled risk information.[223] The plaintiff, therefore, should be able to argue that the risk(s) posed by on-label use was not equally applicable to the relevant off-label use because of *either* the scientific evidence about the risk *or* the nature of the defendant's communication (or a combination of the two).

B. Legal Justifications

Simplifying the preemption framework has three further implications. First, it unifies preemption doctrine across drugs and devices while explaining and preserving the disparate treatment they receive in the context of on-label uses. Second, it helps to show why courts mistakenly find preemption of state law claims based on off-label promotion. And, just like with unification, it does this by demonstrating how this correction is consistent with and supported by Supreme Court precedent. Finally, the approval theory opens what most courts view as a closed window for some state law claims against generic manufacturers based on off-label promotion.

1. DOCTRINAL UNIFICATION

Currently three different preemption frameworks apply to drugs and devices. Express preemption bars all but parallel state law claims against manufacturers of PMA devices. Implied preemption bars state law claims against manufacturers of PMA and 510(k) devices and drugs if they conflict with state law, though apply more expansively to manufacturers of devices than to manufacturers of drugs. This framework is complicated enough. But as Part II showed, courts have further increased

223. For example, one theory of liability for on-label risks is overpromotion. *E.g.*, *Whitley v. Cubberly*, 210 S.E.2d 289, 292 (N.C. Ct. App. 1974).

complexity by applying it in conflicting ways to state law claims based on off-label promotion.

The approval theory, supported by the thoroughness principle, both explains the broader preemption framework for on-label uses and unifies courts' disparate implementations of it as applied to off-label uses for both drugs and devices. It explains the framework by showing how each version of preemption depends on the extensiveness, or thoroughness, of FDA's review. Express preemption applies to PMA but not to 510(k) devices because PMA devices undergo more extensive review than 510(k) devices. This also explains why implied preemption is weaker as applied to 510(k) devices than to drugs, as the latter typically undergo more extensive review than *either* 510(k) or PMA devices. If the purpose of FDA review is to ferret out ex ante risks, then it makes sense to decrease liability for drug and PMA device manufacturers (whose products undergo extensive review) and expand it for 510(k) device manufacturers (whose products undergo less extensive review). The more FDA gathers and reviews (better) information, the less need there is to identify and change the behavior of firms in response to unidentified risks once a drug or device reaches the market.

Besides explaining the coherence of the existing preemption framework, the approval theory also unifies the currently fragmented judicial applications of it by showing why most claims against manufacturers involving off-label promotion should proceed against both drug and device manufacturers. The purpose of preemption in this context is tied to a central function of FDA review, which is ex ante risk regulation of *particular uses* that provides notice to physicians of risks through *approved* labeling. The doctrine avoids conflict between what FDA has done (review) and what state law would otherwise require manufacturers to do (state law liability). In other words, preemption applies because FDA has *thoroughly evaluated* risks of particular, approved uses prior to marketing and provided notice of its evaluation. This makes state regulation of the same risks duplicative and potentially inconsistent with federal regulation. If FDA has not yet done a particular kind of ex ante review, as with off-label uses, the need for the doctrine falls away. Indeed, without FDA approval physicians lack notice of the scope of reviewed risks. State law operates here to ensure notice is provided when off-label promotion occurs.

The upshot of this analysis is twofold. First, it preserves the Supreme Court's preemption jurisprudence by explaining its coherence through FDA's regulatory function. Second, the explanation provides a compelling reason why preemption should not apply to state law claims based on off-label promotion. And because preemption does not apply to claims based on off-label promotion, this approach replaces the entire

morass of preemption analysis described in Section II.C with a much simpler question: Is the basis of the claim off-label promotion? If so, then federal law does not preempt any state law claims *unless* an on-label risk is equally applicable to the off-label use.[224] Preemption, then, generally will not bar state law claims based on off-label promotion unless the risks posed by approved use are equally applicable to the off-label use.

In some cases, however, FDA does review certain off-label risks, even requiring them to appear on the drug label.[225] For these "off-label, on-label" uses, the theory cuts the other way. Here, FDA *has* reviewed off-label uses *and* provided notice to physicians by requiring information on the label. Preemption, therefore, should apply unless the manufacturer promoted a use that involved a risk FDA did not review. For claims based on "new risk information," the existing implied preemption framework under *Wyeth* applies.[226] Failure to warn claims can proceed if the manufacturer failed to update the label under the CBE regulations, unless the manufacturer can show by clear evidence that FDA rejected the change through agency action. Because this preemption framework is based on the same general principle as the approval theory, it does not bar failure to warn claims in these cases based on risks the manufacturer knew about, but FDA had not reviewed. In short, the approval theory also explains why and when these claims can proceed even for labeled, off-label risks.[227]

2. DOCTRINAL MISTAKES

Another advantage of the approval theory is consilience. It not only unites the strands of preemption decisions, but it untangles them as well by showing the critical flaw in decisions finding express or implied preemption. Consider two mistakes in decisions finding express preemption: The first occurs when courts evaluate whether federal requirements apply to a PMA "device." As Section II.C.1 showed, courts universally hold that express preemption applies to an PMA device and not to the uses of the device. State law claims based on off-label

224. This will still require facts substantiating that the use in question was caused by off-label promotion.

225. *See supra* notes 204–07 and accompanying text.

226. It may seem odd to use *Wyeth* because FDA did review the risk at issue. *Wyeth*, 555 U.S. at 558–59. But the framework is still applicable because it is at least possible for manufacturers to update the labeling under the CBE regulation to reflect these risks—something it cannot do for off-label uses generally.

227. One thing the theory may not be able to explain is the preemption of claims against generic manufacturers based on a *brand name* manufacturer's off-label promotion.

promotion, then, can be expressly preempted if they are not parallel to federal requirements.

The problem with this reasoning is that it misreads both the FDCA and *Riegel* by conceptualizing devices as *things* rather than *intended uses* of things. The FDCA, however, defines devices by their intended uses, not by their technical components. A flat plastic stick can be either a tongue depressor or a tool for arts and crafts. A heartrate monitor can detect irregular heartbeats (atrial fibrillation) or track fitness activity for wellness use.[228] What legal category the product falls into, according to the FDCA, depends on the use to which the manufacturer objectively intends it to be put.[229] Manufacturers that promote an off-label use evince an objective intent to use the device for a purpose other than the one for which it is approved. In FDA parlance, it is a "new device"—meaning the FDCA does *not* impose any requirements on the device because it lacks approval.[230] It is also "misbranded" because it lacks "adequate directions for use"—meaning the FDCA can hardly impose requirements on the device that lacks adequate information for uses it has not reviewed.[231]

Riegel's holding, which is consistent with this reasoning, was that PMA imposes requirements that (generally) shield device manufacturers from claims based on uses the manufacturer does not intend (*i.e.*, those that occur during off-label uses the manufacturer has not promoted). The question in *Riegel* was whether the manufacturer could be liable for a physician's mere off-label use. With a nod to the practice of medicine, the Supreme Court answered in the negative. Crucially, it noted that the statutory text erected a liability shield when federal requirements applied to the device, not to the mere off-label use by a physician in the field.[232]

That is correct. Federal requirements *do* apply to the device. But the device in *Riegel* was, as required by the FDCA, defined by its intended

228. It is true that some products may function only as a device—such as an implantable cardiac pacemaker, which is otherwise not very useful except when it is used to regulate the heart in a particular manner—but they need not have only *one intended use or one function*. For example, a pacemaker may be approved for use in patients aged twenty to twenty-five but not seventy to eighty-five. And even an implantable cardiac pacemaker could have other functions, such as tracking and monitoring a user's cardiovascular health or be used as a component in another device that uses the information it generates.

229. *See* David A. Simon, Carmel Shachar & I. Glenn Cohen, *Skating the Line Between Wellness Products and Regulated Devices: Strategies and Implications*, J. L. & BIOSCIENCES, July–Dec. 2022, at 1 (2022).

230. Courts generally do not recognize this. For one that does, see *Ramirez v. Medtronic Inc.*, 961 F. Supp. 2d 977, 995–96 (D. Ariz. Aug. 21), *clarified on denial of reconsideration* (D. Ariz. Oct. 24, 2013).

231. 21 U.S.C. § 352(f); 21 C.F.R. §§ 801.5–.6, .109 (2024).

232. *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 322–23 (2008).

use in the PMA application—its *approved* use. The plaintiff never alleged that the manufacturer intended the off-label use—indeed all the evidence suggested the risk was disclosed in the approved label.[233] And the Court rightly noted that the mere fact that a physician used the device off label, by itself, says nothing about the manufacturer's intent. Understandably, then, the Court concluded that the PMA imposed requirements on the device, by which it meant the device's *intended uses*. Since the off-label use was not an intended use, federal law preempted the claim against the manufacturer premised on the off-label use.

The startling implication of this view is that courts have routinely and wrongly concluded that marketing and design defects, as well as warranty claims, are expressly preempted—both as to drugs and devices.[234] The approval theory helps to both explain the outcome and the rationale that supports it. On this theory, preemption bars state law claims if they are based on *approved uses* and the risks associated them. As part of the PMA process, FDA generally reviews only the risks associated with the intended uses of the product, not all possible uses of it. Highlighting use-dependent determination forces a marriage of FDA's core function to the statutory text: requirements applicable to the device mean requirements imposed by FDA on a product intended for particular uses. When the manufacturer promotes a use other than the one FDA has evaluated, the manufacturer intends a new use that FDA has not yet reviewed.[235] Requirements that applied to the PMA device do not apply to the new one for a very simple reason: FDA has not reviewed the risks of the new device. In this way, the approval theory shows why federal law should not preempt *any* state law claims based on off-label promotion of uses that FDA has not evaluated, including design defect and warranty

233. *Id.* at 320.

234. *E.g.*, *Bertini v. Smith & Nephew, Inc.*, 8 F. Supp. 3d 246 (E.D.N.Y. 2014) (express preemption design defect claim because it applies to the device); *Blankenship v. Medtronic, Inc.*, 6 F. Supp. 3d 979, 989 (E.D. Mo. 2014) (holding design defect claim based on off-label promotion expressly preempted because otherwise state law requirements would interfere with federal ones); *White v. Medtronic, Inc.*, 808 F. App'x *290, *294–95 (6th Cir. 2020) (finding preemption applied to components of a hybrid device when only one component of the device was used in the off-label context). At least in *White*, the finding is puzzling. FDA approves a device as an integrated unit. The fact that a component of an approved device is removed and used should not insulate the manufacturer from liability for that other use. The point of FDA review is to identify risks for the intended use *of the device*—not to uses of components of the approved device in settings not reviewed by FDA. Under this rationale, preemption would protect a manufacturer of a PMA pacemaker that promoted one of its components to be implanted in a patient's brain to reduce symptoms of Parkinson's disease.

235. *E.g.*, 21 C.F.R. §§ 801.4 (defining "intended uses"), 814.80 (prohibiting labeling or advertising other than as approved in PMA).

claims as to the promoted (*i.e.*, intended) use of the product unless the on-label risk is equally applicable to the off-label use.[236]

Yet even if this error was corrected, a second needs to be fixed. When assessing whether state law claims are parallel (under express preemption analysis of PMA devices) or have an independent basis in state law (under the fraud-on-the-FDA implied preemption analysis of devices and drugs), a number of courts confuse the *form* of a federal law violation with the *substance* of a state law violation. For example, some courts hold that off-label promotion is barred by federal law (in some form) but conclude that there is no accompanying state law prohibition on the practice. Off-label promotion, they claim, is wholly a creature of federal law with no state law analogy. In short, they require identity, rather than equivalence, of claims.[237]

But the question is not whether state law prohibits the identical *named* conduct.[238] The question is whether the federal and state law prohibit the same *kind* of conduct. Claims based on off-label promotion do not assert that the wrong consists of the category of speech called off-label promotion. Instead, they claim that promoting a use off label violated a parallel state law duty *based on the same substantive conduct*, such as the duty to provide adequate warnings. Pointing to the absence of a state "law" barring off-label promotion shows only that states do not have laws identical to federal ones, not that they lack "parallel" state laws. The fact that state law duties prohibit, for example, products that contain marketing or design defects is sufficient to state a parallel claim based on conduct that also serves as the basis for violations of federal law. Precise identity in the *descriptions* of the claim is irrelevant.

Reframed this way, allegations of off-label promotion can parallel state law claims with an independent pre-existing legal duty, such as those for failure to warn, quite easily. The parallel state law duty is to provide adequate warnings or non-defectively designed products. And common law duties in products liability law, like failure to warn, generally predate the MDA. A manufacturer that promotes an off-label use incurs a duty to warn of the risks of that use.

Like in the context of express preemption, the approval theory in the context of implied preemption provides a normative justification for

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236. Because express preemption does not apply at all, this avoids decisions holding that state laws are not parallel laws because they command conduct where a federal law merely permits it. *E.g.*, *In re Medtronic, Inc., Sprint Fidelis Leads Prod. Liab. Litig.*, 623 F.3d 1200, 1205 (8th Cir. 2010).

237. Judge Lucero makes this point well in his *Caplinger* dissent. *Caplinger v. Medtronic, Inc.*, 784 F.3d 1335, 1351–56 (10th Cir. 2015) (Lucero, J., concurring in part and dissenting in part).

238. Some statutes actually exempt manufacturers from liability resulting from "truthful promotion of off-label uses" *E.g.*, TENN. CODE ANN. § 53-10-113 (2024).

allowing state law claims based on off-label promotion to proceed as parallel. FDA has not reviewed the risks associated with the promoted off-label uses. Indeed, the whole purpose of federal laws prohibiting off-label promotion is to regulate manufacturer conduct ex post. In short, the federal law prohibits conduct *after* FDA review.[239] This is precisely the kind of conduct state law should regulate because FDA cannot.

Here a question of scope arises. As presented so far, the approval theory would allow all state law based on off-label promotion claims because (1) express preemption does not apply; and (2) the conduct prohibited by federal law corresponds to a preexisting independent state law duty.[240] But how far does (2) extend?

The question is fundamentally about how strict the equivalence between federal and state law must be for a claim to proceed. If federal law bars off-label promotion, defined only as false or misleading speech, then must state law mirror those requirements exactly with preemption barring all but fraud-type claims?[241] Or, can state law duties include causes of action not prohibited by federal law?

The approval theory suggests that the bounds of a federal prohibition do not necessarily demarcate state law claims. Put differently, state law claims can include a broader class of conduct than explicitly prohibited by federal law. If the purpose of preemption is to ensure only FDA polices ex ante risks, then it does not follow that states should refrain from policing ex post ones, including risks that federal regulations do not specifically enumerate.[242] Requiring identity between federal and state law duties would essentially impose a parallel claims requirement on implied preemption, collapsing the distinction between express and implied preemption.

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239. This reasoning surfaces when courts hold federal law does not preempt express warranty claims. *Wildman v. Medtronic, Inc.*, 874 F.3d 862, 868 (5th Cir. 2017) ("When the promise was one the FDA approved, tort liability for breaking it would conflict with the FDA's view that the representation was a sound one. So when a claim challenges a representation the FDA blessed in the approval process, it is preempted."). *See also Cipollone v. Liggett Grp., Inc.*, 505 U.S. 504, 526–27 (1992) (plurality opinion) (finding express warranty claims not expressly preempted because did not arise "under state law" but rather by the terms of the warranty itself).

240. The prohibited conduct here is not engaging in speech but rather the act of shipping a new or misbranded device. 21 U.S.C. §§ 331(a)–(b).

241. *See* cases cited *supra* note 188.

242. *Wyeth v. Levine*, 555 U.S. 555, 579–81 (2009) (discussing the general statutory language and comparing it to specific rulemaking). The situation might be different if FDA adopted specific off-label speech regulations, as it once did. *See* 21 U.S.C. §§ 360aaa, 360aaa-1 (sunset in 2006). For a decision discussing these now sunset code provisions and related regulations, see *Riley v. Cordis Corp.*, 625 F. Supp. 2d 769, 781–82 (D. Minn. 2009).

Doctrinally, there are also strong reasons supporting the approval theory's approach. *Wyeth* teaches that complementary state law enforcement regimes do not necessarily present an obstacle to, or enforcement of, the federal scheme.[243] Nor is it impossible to comply with federal and state requirements where federal law is silent on the conduct.[244] This is true even for failure to warn claims under the CBE regulations, which *permit* but do not require manufacturers to voluntarily update their labels.[245] Tort law here does not conflict but instead acts as an additional incentive for manufacturers to do what federal law otherwise permits them to do: update risk information as fast as possible by changing the label. Similarly, a federal prohibition on false or misleading, but not negligent, off-label promotion would not bar suits based in negligence. Here a lawsuit would serve the same function as in *Wyeth*: it would supplement federal regulation, incentivize risk disclosure, and compensate injured patients. All this is buttressed by the fact that FDA's primary function is to review risks ex ante and decide which are worth disclosing—something it has not yet done, or done in the same way, with respect to off-label uses.[246]

3. Liability of Generic Drug Manufacturers

State law claims against generic manufacturers pose unique challenges that the approval theory is equipped to handle. First, claims

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243. *Wyeth*, 555 U.S. at 578–79.

244. This is not the case in express preemption.

245. *E.g.*, *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1678–79 (2019).

246. What is essential to recognize for implied preemption purposes is that off-label promotion can form the basis of a state law claim even if it does not violate the federal law. Unlike express preemption, there is no requirement that state law claims parallel federal ones—imposing one would collapse implied preemption and express preemption into each other. Implied preemption's relevant forms require only that the state law obligation cannot present an obstacle to a federal legislative scheme or make compliance with both impossible. But if federal law does not bar the conduct, and FDA has limited jurisdiction over off-label promotion, that is an argument for, not against, the state law as a "complementary form of drug regulation." Unlike the on-label context, warning of risks when promoting off-label is not prohibited because it does not constitute a change to the drug label (at least if off-label promotion is not prohibited). Hence, complying with state law requirements in such circumstances is not impossible because there are no federal requirements. State law claims against manufacturers, on this view, can hardly be said to constitute an obstacle to the federal statutory scheme if the conduct is not prohibited and the behavior is disfavored by FDA. Here the FDCA's regulatory structure may actually be strengthened, rather than inhibited, by delegating to state law an area that FDA has had difficulty policing and where state law verdicts are perfectly consonant with FDA regulation. There remain unresolved issues regarding the First Amendment that are not discussed further here. *See* Simon, *supra* note 19.

against generic manufacturers are often based on off-label promotion by the brand name manufacturer rather than the generic manufacturer. Suing the generic manufacturer for actions of the brand name manufacturer presents a unique situation that does not easily fit standard tort and contract doctrines. Second, and perhaps more importantly, courts have generally extended the rationale of *Mensing* and *Bartlett*—which held that federal law will impliedly preempt failure to warn and design defect claims against generic manufacturers because they cannot unilaterally change the drug label—to cover *any* off-label speech.[247]

This opens a liability gap when the brand manufacturer promotes off-label, but the generic causes the harm: the generic is immune from suit because, although brand manufacturer's off-label promotion caused the prescription, the generic drug caused the injury.[248] The result may be the same when the generic promotes the drug off label.

Unifying the doctrine through the approval theory, however, offers a rationale creating another "narrow gap"—this time through *Mensing* and *Bartlett*—for avoiding implied preemption. By focusing on ex ante risk regulation, one can immediately see that off-label promotion claims against either generics or brand name manufacturers should proceed—for many of the same reasons as stated above.

The doctrinal reason at least some of these claims should go forward is related. To see why, consider that cases finding federal law preempts off-label promotion claims against generics generally hold that any communication would constitute "labeling."[249] Yet at least one line of cases holds that at least some of this communication is protected by the First Amendment, presenting a challenge to prosecution and potentially civil liability of truthful off-label speech. This protection may actually *invite* failure to warn claims against generics.[250] If generics cannot violate the misbranding provision of the FDCA by providing truthful off-label speech, then they *can* be held liable for an activity that the FDCA allows.

Put differently, if the FDCA allows truthful off-label speech, it also allows communication of truthful risk information. If it did not, this would mean that drug companies would be allowed to provide information about the benefits of a drug but prohibited from communicating information about its risks. It would be odd if manufacturers did *not* have such a duty—and could instead provide

247. *PLIVA, Inc. v. Mensing*, 564 U.S. 604 (2011); *Mut. Pharm. Co. v. Bartlett*, 570 U.S. 472 (2013). *See also* cases cited *supra* note 154.

248. *Mensing*, 564 U.S. at 617–19; *Bartlett*, 570 U.S. at 480. *See also* cases cited *supra* note 210.

249. *E.g.*, *Polt v. Sandoz, Inc.*, 462 F. Supp. 3d 557, 564–65 (E.D. Pa. 2020).

250. *Cf. Kellogg v. Wyeth*, No. 07-cv-82, 2012 WL 368658, at *5 (D. Vt. Feb. 3, 2012) (holding *Mensing* foreclosed this claim).

information about only the purported benefits of an off-label use. Liability attaches here by failing to communicate off-label risks in protected speech activity. The same rationale applies to generics. If the government cannot prosecute a brand manufacturer because it is allowed to communicate off-label information, then the same is true for the generic manufacturer.[251]

Importantly, generic manufacturers under this system are *not* faced with a stop-selling ultimatum that drove the arguments for preemption forward in *Mensing* and *Bartlett*. They can continue to sell their products by providing truthful information about off-label risks in the same way firms provide truthful information about off-label uses. Requiring generic manufacturers to provide such information does not impose some additional duty—it is part and parcel of the duty to warn. And tort law makes sure that this duty is commensurate with the manufacturer's ability to learn about risks; it will not impose liability for risk the manufacturer did not or could not have known about. Under this rule, generic manufacturers will not be held liable for failing to disclose of risks known only to the brand manufacturer—they will be liable for failing to warn only of risks they knew or should have known about. While requiring generic manufacturers to disclose off-label risks may not be the most efficient or desirable strategy, it is one the law allows. And with Congress or FDA unwilling to amend the FDCA or its accompanying regulations, it is the one that the courts should follow.[252]

C. Policy Justifications

While the approval theory is aptly supported by doctrine, there are also strong policy reasons to support a preemption rule that allows tort claims to proceed, including correcting for informational asymmetries, deterring manufacturers from engaging in harmful off-label promotion,

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251. The case may be different when *no* off-label speech is allowed, because then the generic must violate federal law to comply with the state law duty. If the generic manufacturer is not promoting the use off label and its communication of risk information would violate federal law, then *Mensing* and *Bartlett* would likely preempt this claim. Here the approval theory cannot help, though it suggests that perhaps some other aspect of the law should be changed or damages against the brand manufacturer increased. However, it is difficult to see FDA prosecuting a drug or device manufacturer for providing additional warnings.

252. In 2013, FDA proposed a rule that would have allowed generic drugmakers to update their labels with off-label risks. Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67985, 67989–91 (Nov. 13, 2013). But it abandoned the rule in 2018. Withdrawal of Proposed Rule on Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 83 Fed. Reg. 64299, 64301 (Dec. 14, 2018).

compensating injured patients, holding manufacturers morally responsible, and preserving innovation.

1. INFORMATION ASYMMETRY

The approval theory corrects for information asymmetries—a core reason for laying at the feet of manufacturers duties related to product manufacturing, design, and warning. Manufacturers have better information than the physicians to whom they are marketing a drug or device.[253] This is doubly true for off-label uses manufacturers promote. Physicians are busy and susceptible to marketing and, depending on practice area, may have little familiarity with the off-label use or the evidence supporting it.

Some courts have, rather curiously, argued that state law liability for off-label promotion "illegitimately shifts the risk of off-label use from prescribing doctors and patients to manufacturers."[254] While this may be true in cases where the manufacturer neither intends nor can foresee the off-label use, it does not apply to cases where the manufacturer promotes the use in question. If the manufacturer is promoting an off-label use, it both foresees and intends the use. It should, therefore, bear the risk of the promoted use, including injuries that result from marketing and design defects.[255] Courts repeatedly recognize that manufacturers are likely to have the best and most current information about their drugs and devices,[256] and that they are the cheapest cost-avoider.[257] Contrary to the language quoted above, physicians, hospitals,[258] and patients should not assume the risk when a manufacturer encourages them to take risks without providing sufficient information to make an informed decision about whether the risk is worth taking.

Manufacturers, then, should be liable under state law for harms that result from off-label promotion because they are in the best position to

253. *See Wyeth v. Levine*, 555 U.S. 555, 578–79 (2009).

254. *Clements v. Sanofi-Aventis, U.S., Inc.*, 111 F. Supp. 3d 586, 601 (D.N.J. 2015) (citing *Caplinger* favorably).

255. It is also in a better position to spread the costs of these risks. Helveston, *supra* note 14, at 1136.

256. *E.g.*, *Wyeth*, 555 U.S. at 578–79; *Colacicco v. Apotex Inc.*, 521 F.3d 253, 282 (3d Cir. 2008) (Ambro, J., dissenting), *vacated*, 556 U.S. 1101 (2009). *See also Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 451 (2005).

257. *See generally* GUIDO CALABRESI, THE COSTS OF ACCIDENTS: A LEGAL AND ECONOMIC ANALYSIS (1970).

258. Several cases have held that the duty to warn extends beyond physicians to institutions that purchase medical devices. *E.g.*, *Taylor v. Intuitive Surgical, Inc.*, 389 P.3d 517, 525–26 (Wash. 2017); *Noorchashm v. Muto*, No. 1584CV03245, 2021 WL 3612425, at *6 (Mass. Super. Ct. July 8, 2021).

provide information about the risks and benefits of the promoted off-label use. Additionally, the manufacturer can provide appropriate information—whether it is warnings or contextual information—at the cheapest cost.[259] Until FDA reviews (and makes decision about) the specific risks associated with the promoted off-label use, the manufacturer should be responsible for communicating risk information.

2. DETERRENCE

No law, however perfect, can prevent all injuries. But a central premise of the legal system is that potential liability can influence behavior. How much influence the law has depends on a variety of factors, including the severity of injuries and the number of patients injured. But there are reasons to think that, at least for some claims, liability for off-label promotional activities that injure patients would have a significant impact.

To see why, consider the costs of widespread, or mass tort, cases where litigation costs can run in the billions. One example is the lawsuits against the manufacturers of phentermines Pondimin and Redux, known as the "Fen-phen" litigation.[260] Plaintiffs brought "tens of thousands" of cases alleging a number of claims, typically under failure to warn theories but also under theories that the company willfully withheld risk information.[261] The cost of these lawsuits has been close to $20 billion.[262] To put that in perspective, the drug's total sales for 1996 were $305 million.[263]

To date, private lawsuits based on off-label promotion have focused on major players in the drug and device space, including Medtronic, Sanofi, and Pfizer. Many of these cases have been dismissed on preemption grounds, telegraphing to others that such claims will not affect their profit margin. Contrary holdings could bolster efforts to curb harmful off-label promotion by providing a disincentive to promote off label.

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259. Kaspar J. Stoffelmayr, Comment, *Products Liability and "Off-Label" Uses of Prescription Drugs*, 63 U. CHI. L. REV. 275, 289 (1996).

260. STEVEN GARBER, RAND CORP., ECONOMIC EFFECTS OF PRODUCT LIABILITY AND OTHER LITIGATION INVOLVING THE SAFETY AND EFFECTIVENESS OF PHARMACEUTICALS 28 (2013).

261. *Id.* at 28–30.

262. *Id.* at 30.

263. *What's the "Skinny" on Fen-Phen?*, FINDLAW (July 7, 2017), https://corporate.findlaw.com/litigation-disputes/what-s-the-skinny-on-fen-phen.html [https://perma.cc/JHA8-CZLZ].

3. COMPENSATION

Civil law directed at personal injuries serves as an important social safety net for those harmed. It allows individuals to recover at least some of costs incurred as a result of another's conduct. For those injured by drugs or devices, these harms may be significant. They may lose limbs or the ability to walk. Others may require reoperation.[264] Some may die.[265] To the extent that tort liability provides compensation for injuries caused by off-label promotion, it helps patients deal with the cost of socially undesirable behavior that the law did not deter. Compensation also validates patient injuries and provides patients the chance to hold tortfeasors responsible for their conduct. Benefits like these fortify the legitimacy of the legal system.

4. CULPABILITY

Liability under state law for harms caused by off-label promotion is also appropriate because the manufacturer is responsible for the harm it caused.[266] Promoting a use off-label generates additional profits for the manufacturer. Although manufacturers frequently engage in off-label promotion to increase sales, they may also do it to bring therapies to patients that would otherwise have none. Holding them responsible for the consequences of their actions does not require attributing to them nefarious motives. They are aware of the risks of their behavior and are therefore responsible for the results. Where, however, they are driven primarily by profit without sufficient evidence, or even in spite of it, they are morally culpable for their actions. They can, of course, absolve themselves of culpability by applying to FDA for approval or clearance of their drugs or devices or by not promoting off-label uses in ways that violate the law.

5. INNOVATION

Courts sometimes justify a finding of preemption by arguing that private state law claims based on off-label promotion may chill innovation. Consider one court's argument that subjecting manufacturers to "fifty states' warning requirements concerning off-label uses, on top of existing federal on-label warning requirements, might introduce

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264. *E.g.*, *Funke v. Sorin Grp. USA, Inc.*, 147 F. Supp. 3d 1017, 1028 (C.D. Cal. 2015) (discussing Funke's allegations).

265. *E.g.*, *Hill v. Abbott Lab'ys*, No. 19-cv-01011, 2020 WL 4820243, at *1 (D.S.C. Aug. 19, 2020).

266. This responsibility may imply moral desert.

sufficient uncertainty and cost that manufacturers would delay or abandon at least some number of life-saving innovations."[267]

This argument has several problems. First, it probably overestimates the uncertainty that off-label promotion claims would generate. Looking at existing state and federal decisions, for example, reveals much of the disagreement about state law claims is not around the uncertainty of the claims' success but rather whether those claims are preempted. In other words, preemption itself creates the uncertainty it purports to eliminate. If courts are unified in their approach to preemption, the variations between states on say, warning requirements, may be less significant than those that exist today with respect to preemption.[268]

Second, it confuses the incentive to seek FDA approval with the ability to promote off-label uses. FDA approval requirements generate incentives to develop data demonstrating a drug is safe and effective for particular uses.[269] Firms have an incentive to obtain approval to market their drug because it allows them to sell and market it for the particular uses the manufacturer has validated. If manufacturers can promote off-label uses without validating them and increase sales, this reduces a firm's incentive to pursue "at least some number of life-saving innovations."[270] Rather than generate more innovation, off-label promotion is likely to reduce it.[271]

Third, the argument overconfidently predicts that regulatory uncertainty would reduce innovation. Regulatory uncertainty, of course, can affect how firms invest and innovate.[272] Uncertainty with respect to some legal rule relating to drug and device manufacturer liability, however, does not guarantee that this uncertainty will reduce innovation. Quite the opposite may be true.[273] It all depends on the tradeoffs in the new system and the benefits reaped by trading the costs of one system for another. Prophesized negative spillover effects (caused by states

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267. *Caplinger v. Medtronic, Inc.*, 784 F.3d 1335, 1346 (10th Cir. 2015).

268. This argument would have more force, though would still be deficient, if a unified approach to preemption existed.

269. *See* Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. TECH. L. REV. 345, 385 (2007); Erika Lietzan, *Paper Promises for Drug Innovation*, 26 GEO. MASON L. REV. 168, 172 (2018).

270. *Caplinger*, 784 F.3d at 1346 (citing a number of articles by Catherine Sharkey, including "Products Liability Preemption," *supra* note 14).

271. The term "innovation" is general—perhaps purposefully so. It may mean just more new stuff. Or it may mean more new stuff that works. At least for drugs and devices, it likely means, at a minimum, discovering and validating safe and effective drugs and devices.

272. *E.g.*, Jaime Bonnin Roca & Eoin O'Sullivan, *The Role of Regulators in Mitigating Uncertainty Within the Valley of Death*, TECHNOVATION, Jan. 2022, at 1, 1–3.

273. *See id.* at 9.

overcompensating and exporting regulation to out-of-state companies),[274] for example, may be countered by positive ones (decreasing improper off-label promotion and prescribing).[275]

Additionally, spillovers do not simply occur bidirectionally in a new system. Imposing liability must be evaluated against its alternatives. One of these is preemption of all state law claims based on off-label promotion. The costs of not allowing state law claims are significant. Injured patients suffer real physical and financial costs, and their injuries reverberate throughout the healthcare system. Failure to impose liability on manufacturers who improperly promote off-label may also further degrade trust in FDA and, possibly, the legal system. Perhaps more significantly, it enables manufacturers to influence the standard of care in ways that seem antithetical to the practice of evidence-based medicine.[276] And, as noted above, it removes a potential deterrent for socially undesirable behavior. What is more, while off-label innovation is not infrequent, it is physicians who are innovating, raising questions about the innovative value of off-label promotion.

Whatever the actual effects on innovation or state behavior, they are not clear in advance. States could race to the bottom or the top, with correspondingly different effects nationwide. Firms could abandon innovative off-label treatments or simply abandon marketing them prior to approval. So while it is true that eliminating preemption will create some uncertainty, the question is whether these uncertainties are worth accepting given the nature of the harm caused by improper off-label promotion.

Without FDA reviewing off-label risks and notifying physicians of them in the same way as it does for on-label risks, the case for state law looks quite strong. Filling in this regulatory hole is what states should be

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274. *Caplinger*, 784 F.3d at 1346–47 ("Regulating any aspect of a device also raises the possibility of 'spillover effects' from rules that 'benefit in-state residents' at the expense of out-of-staters. In short, we can see a number of ways in which a lawsuit nominally limited to attacking an off-label use might have knock-on effects for those seeking access to a device for its on-label use." (citation omitted) (quoting Samuel Issacharoff & Catherine M. Sharkey, *Backdoor Federalization*, 53 UCLA L. REV. 1353, 1386–87 (2006))). The court misunderstands Issacharoff and Sharkey's argument. They did not argue that spillover effects are always bad, only that national standards attempt to resolve the spillover dilemma by imposing uniform rules. Issacharoff & Sharkey, *supra*, at 1386–89. These rules, of course, can also be over- or under-regulated. More importantly, however, the question of whether preemption should apply to claims generally is different than whether there should be any room for tort law within a preemption framework.

275. *Caplinger*, 784 F.3d at 1336–37 (noting the possibility of under- or over-regulation).

276. Ani B. Satz & Liza Vertinsky, *Customary Corruption*, 66 WM. & MARY L. REV. (forthcoming 2025).

doing in the absence of use-based risk information reviewed by FDA.[277] And it is precisely the kind of activity the Supreme Court has found to be the provenance of state law in the context of drugs and devices.

D. Beyond Preemption

Preemption is a litmus test. Overcoming it does not mean all claims against drug and device manufacturers will succeed. This Section briefly sketches several salient issues that will arise if the approval theory eliminates the preemption defense for state law claims based on off-label promotion.

The first is Comment k of the Restatement of Torts, which provides a limited defense of strict liability claims for "unavoidably unsafe products," such as prescription drugs that are "incapable of being made safe for their intended and ordinary use."[278] To avoid strict liability, the unavoidably unsafe product must be "properly prepared, and accompanied by proper directions and warning."[279]

Courts that follow Comment k frequently hold it applies to prescription drugs.[280] Some also hold it applies to prescription devices.[281]

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277. *Contra Caplinger*, 784 F.3d at 1346–47.

278. RESTATEMENT (SECOND) TORTS § 402A cmt. k (AM. L. INST. 1965).

279. *Id.*

280. Some courts apply it to all prescription drugs. *E.g.*, *Brown v. Super. Ct.*, 751 P.2d 470, 477 (Cal. 1988); *McKee v. Moore*, 648 P.2d 21, 24 (Okla. 1982); *Young v. Key Pharms., Inc.*, 922 P.2d 59, 64 (Wash. 1996) (en banc) ("[U]nder Washington law, a separate determination of whether a product is unavoidably unsafe need not be made on a case-by-case basis if that product is a prescription drug."). *See also Carlin v. Super. Ct.*, 920 P.2d 1347, 1355 (Cal. 1996) (noting that *Brown* did not foreclose warning defect and implied warranty claims). Others apply it on a case-by-case basis. There is, of course, considerable disagreement about how it ought to apply. For a discussion of the provision, its revision, and cases citing it, see James A. Henderson, Jr. & Aaron D. Twerski, *A Proposed Revision of Section 402A of the* Restatement (Second) of Torts, 77 CORNELL L. REV. 1512 (1992).

281. *Aaron v. Medtronic, Inc.*, 209 F. Supp. 3d 994, 1012–14 (S.D. Ohio 2016) (holding that under Ohio law, which had adopted comment k, a PMA device was "an unavoidably unsafe product" and subject to comment k); *Keen v. C.R. Bard, Inc.*, 480 F. Supp. 3d 624, 635 (E.D. Pa. 2020) ("The Pennsylvania Supreme Court has yet to specifically address comment k's application to prescription medical *devices*. . . . [But] many district courts applying Pennsylvania law have similarly predicted that the Pennsylvania Supreme Court would likely extend its bar of strict liability of prescription drug claims to prescription medical device claims."); *Gross v. Stryker Corp.*, 858 F. Supp. 2d 466, 482 (W.D. Pa. 2012) (citing similar cases from courts within the Third Circuit cases and holding "the inherently rigorous nature of the premarket approval process . . . suggest[s] that the Trident System is an 'unavoidably unsafe' product to which strict liability does not apply" and comment k does); *Adams v. G.D. Searle & Co.*, 576 So.2d 728, 733 (Fla. Dist. Ct. App. 1991) (explaining that comment k applies to prescription drugs on a case-by-case basis because of language, drafting history, and

Like many legal issues, however, views are not uniform.[282] Regardless of whether it applies to drugs or devices, the general thrust of the rule is the same: proper manufacturing and warnings preclude strict liability design defect claims.[283] Disputes of the scope and importance of this provision vary, with some claiming it preserves a distinction between strict liability and negligence and others noting that most strict liability warning and design defect claims are essentially negligence claims.[284] Complicating matters further, Comment k does not necessarily foreclose claims sounding negligence even if it applies.[285]

Courts already have experience applying Comment k, but it is not clear how they would evaluate its impact in off-label promotion cases. While the precise scope of the rule and its application are a constant source of debate and disagreement, the rule itself was premised on the same general idea as preemption: manufacturers that properly manufacture and adequately label their product should not be subject to liability if the product causes some harm. This raises the question of whether it applies, and to what degree, to uses that FDA has not reviewed. Courts will be called on to interpret what constitutes "proper direction and warnings," which may more often than not be an issue for the jury rather than the judge.

The second significant issue is the First Amendment. Off-label promotion, while technically illegal, may include truthful speech

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policy underlying the rule). *But see Hricik v. Stryker Biotech, LLC*, 89 F. Supp. 3d 694, 701–02 (E.D. Pa. 2015) (noting fraud claims with an "overt act[]" are not subject to comment k).

282. *E.g.*, *Burton v. Danek Med., Inc.*, No. CIV.A. 95-5565, 1999 WL 118020, at *7 (E.D. Pa. Mar. 1, 1999) ("Section 402A is inapplicable to prescription drugs."). Comment k was adopted primarily to cover liability risks faced by prescription drugs that would have already gone through the approval process. *See* Joseph A. Page, *Generic Product Risks: The Case Against Comment k and for Strict Tort Liability*, 58 N.Y.U. L. REV. 853, 864–66 (1983).

283. RESTATEMENT (SECOND) TORTS § 402A cmt. k (AM. L. INST. 1965). Strict liability and negligent design defect claims, while conceptually distinct, are analytically quite similar.

284. Courts, to be sure, still distinguish the two. *Brown*, 751 P.2d at 476 n.4. For a review of the difference and how courts apply it, see Henderson & Twerski, *supra* note 78, at 271–89.

285. *See, e.g.*, *Keen*, 480 F. Supp. 3d at 640–46 (E.D. Pa. 2020) (finding comment k bars strict liability claims in tort and implied warranty of merchantability claim but not negligent misrepresentation, manufacturing, design, and warning claims). *Taupier v. Davol, Inc.*, 490 F. Supp. 3d 430, 440 (D. Mass. 2020) (holding comment k does not bar implied warranty claims). Massachusetts does not have strict products liability claims in tort. *Phillips v. Medtronic, Inc.*, 754 F. Supp. 2d 211, 216 (D. Mass. 2010) (citing *Commonwealth v. Johnson Insulation*, 682 N.E.2d 1323, 1326 (Mass. 1997)).

protected under the First Amendment.[286] Claims against manufacturers that allege defective marketing or design will have to overcome not just Comment k, but also the potential that their claims may be barred by the First Amendment.

While the bounds of protected off-label speech are still uncertain, recent cases suggest that it is more expansive than FDA assumed. In short, truthful off-label information may be entitled to greater protection from governmental regulation than false or misleading speech, which the government can regulate freely.[287] While some attorneys seem to deliberately couch their off-label promotion claims in the language of "false and misleading" to avoid First Amendment hurdles, this language may relegate the ambit of potential claims to fraud-based actions where heightened pleading requirements present significant obstacles.[288] At the very least, there are significant open questions about the extent to which off-label jurisprudence in the criminal context will be applied in the civil context.[289]

The third issue is the potential growth of new claims against drug and device manufacturers, both in quantity and type. The quantity of claims is likely to increase without a preemption defense, though it may be modulated by how courts apply both Comment k and First Amendment protection. The net effect of this increase is unclear. Most likely, several bellwether cases will likely set a new equilibrium for off-label promotion. Firms then must decide whether decide that is a cost they are willing to bear and the cost at which they are willing to bear it. Assuming the bellwether cases involve mass torts, the cost of not changing behavior is likely to be too high to stomach.[290] To respond to new liability exposure, firms will likely decrease the quantity or type of off-label promotion they engage in, though the degree of change is not clear.

Besides the predictable flow of claims, however, firms may also face old-but-unused and new theories of liability. Claims that have lain fallow, such as overpromotion,[291] are likely to be revived and

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286. *See generally* Simon, *supra* note 19.

287. *See id.* at 558–77.

288. *See supra* note 91 and accompanying text; *Hawkins v. Medtronic, Inc.*, 62 F. Supp. 3d 1144, 1153 (E.D. Cal. 2014); *Byrnes v. Small*, 60 F. Supp. 3d 1289, 1298 (M.D. Fla. 2015) (dismissing fraud-based claims because of defective pleading). *See* Beck, *supra* note 21, at 76 & n.406.

289. *E.g.*, *Hawkins*, 62 F. Supp. at 1153 & n.4 (citing differing approaches from courts in the Ninth Circuit); *Carson v. Depuy Spine, Inc.*, 365 F. App'x 812, *815 (9th Cir. Feb. 16, 2010) ("Therefore, while doctors may use a drug or device off-label, the marketing and promotion of a Class III device for an unapproved use violates Section 331 of the FDCA.").

290. *See* GARBER, *supra* note 260, at 28–30.

291. *E.g.*, *Salmon v. Parke, Davis & Co.*, 520 F.2d 1359, 1362 (4th Cir. 1975).

reformulated by enterprising counsel. Additionally, plaintiffs' counsel and scholars are likely to develop innovative theories of liability that aggregate claims and generate significant damage amounts.[292]

CONCLUSION

Common conditions like chronic pain and arthritis of the hip or spine frequently require medication or surgery. Many of the drugs or devices prescribed, administered, or used to treat these conditions will be for uses FDA has not reviewed for safety and effectiveness—off-label uses. Evidence suggests that while the practice is medically necessary and useful in practices like rare diseases, oncology, and pediatrics, off-label use is more likely to be harmful than on-label use. And the harms can be significant, including cancer, paralysis, and even death.

This Article sought to partially reduce these harms by discouraging drug and device companies from promoting off-label uses that are likely to injure patients. The argument was simple: where a drug manufacturer promotes an off-label use that injures a patient, the manufacturer should be liable for that injury if it violated state law.

While straightforward, the argument was complicated by the doctrine of federal preemption, under which federal law can displace state law claims when either Congress directs or the laws conflict. Attempts to address both situations have resulted in conflicting and inconsistent application of the doctrine to claims based on off-label promotion. Sometimes claims are allowed; sometimes they are preempted, with rationales and outcomes varying across and within jurisdictions.

To unify and simplify the preemption inquiry, this Article argues for an approval theory that focused on FDA's core function: ex ante risk evaluation. A central function of preemption is meant to preserve FDA's ex ante risk review from judicial second-guessing. Since FDA does not review risks of off-label uses at all or in the same way it reviews and notifies physicians of on-label ones, preemption should not apply to state law claims against manufacturers for off-label promotion.

By developing this theory, the Article made two significant contributions. First, it comprehensively mapped and compared preemption jurisprudence for on- and off-label uses. Second, it used this mapping to untangle preemption jurisprudence, initially by illustrating the key doctrinal mistakes courts have made that distorted the legal landscape, and then by showing the broader policy reasons supporting

292. For a new theory of liability, see David A. Simon, Off-Label Inducement (unpublished manuscript) (on file with author).

the theory. While this easy-to-use framework swept away the complications posed by preemption, courts will still have to address issues under state law and the First Amendment—issues future scholarship should address.

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