MARKETING AUTHORIZATION AT THE FDA: PARADIGMS AND ALTERNATIVES

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In many critical industries, the Food and Drug Administration's (FDA's) marketing authorization decisions determine the range of products available in the United States. Because of the broad scope of the FDA's marketing authorization responsibilities, the existing scholarship focuses on individual product categories, or small groups of product categories, regulated by the Agency. This Article identifies how the existing literature overlooks important connections between the FDA's different marketing authorization programs. These connections suggest both explanations for existing programs and strategies for potential reforms.

The Article sets forth a two-level framework for analyzing the FDA's marketing authorization role. At the first level, the framework divides the FDA's marketing authorization programs into three components: pathways, designations, and means of access before marketing authorization. At the second level, the framework distinguishes between two types of pathways, three types of designations, and four means of access before marketing authorization. This framework gives a coherent intellectual structure to a sprawling set of regulatory programs that are otherwise difficult to analyze. Based on this framework, the Article makes several analytical contributions specific to food and drug regulation.

The Article's final contribution highlights a newly identified phenomenon, interchangeable-part lawmaking (IPL), that should be of broader interest. IPL takes place when a government entity takes a portion of its law in one subject area and uses it as a model for its own law in another subject area. It is strikingly visible in the statutes administered by the FDA, but IPL likely exists in statutes more generally. IPL has substantial implications for statutory interpretation, as well as for numerous strands of academic literature.

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INTRODUCTION

The U.S. Food and Drug Administration (FDA) is one of the core public health agencies in the United States. It administers a $6 billion annual budget and is charged with regulating industries that, together, comprise a large segment of the U.S. economy.[1] The FDA's highest profile activity is its marketing authorization role.[2] In many industries—such as drugs, medical

1. *See* AGATA BODIE & AMANDA K. SARATA, CONG. RSCH. SERV., R44576, THE FOOD AND DRUG ADMINISTRATION (FDA) BUDGET: FACT SHEET 2, 4, 8 (2021) (describing total enacted fiscal-year 2021 budget, including both congressional appropriations and congressionally approved user fees). For fiscal year 2023, the Biden Administration has proposed an increase of the U.S. Food and Drug Administration's (FDA's) annual budget to over $8 billion. *See* U.S. DEP'T OF HEALTH & HUM. SERVS., FISCAL YEAR 2023 BUDGET IN BRIEF 18–19 (2022).

2. As in the author's prior work, this Article uses "the term *marketing authorization* to refer generally to all processes by which [the FDA] permits products to be marketed in the United States." *See* ADAM I. MUCHMORE, FOOD AND DRUG REGULATION: A STATUTORY APPROACH 81 (2021). Congress, the FDA, and other academics have at times used the term in a similar sense. *See, e.g.*, Federal Food, Drug, and Cosmetic Act (FFDCA) § 802, 21 U.S.C. § 382(b) (use by Congress); 21 C.F.R. pt. 801 (use by the FDA); Sam F. Halabi, *The Drug Repurposing Ecosystem: Intellectual Property Incentives, Market Exclusivity, and the Future of "New" Medicines*, 20 YALE J.L. & TECH. 1, 46, 53 (2018) (use by other academics). This Article prefers marketing authorization rather than the catchier term "gatekeeping" because of the specific meaning the latter term has come to have in the legal literature. Professor Reinier Kraakman used the term "gatekeeper liability" to describe

devices, and biological products—the FDA is the primary agency charged with determining which of those products may be sold in the United States.[3]

Because of the broad scope of the FDA's marketing authorization responsibilities, most existing scholarship focuses on individual product categories, or small groups of product categories, regulated by the FDA. There is no existing agency-wide analysis of the FDA's marketing authorization programs. This is, in part, because the language and conceptual structure necessary for such an analysis does not yet exist. This Article begins to fill that gap.[4] In the process, it demonstrates that the siloed nature of existing scholarship misses important connections between the FDA's various marketing authorization programs.[5]

This Article presents the FDA's marketing authorization activities through a two-level framework.[6] At the first level, the framework divides the FDA's marketing authorization programs into three components: pathways, designations, and means of access before marketing authorization. At the second level, the framework distinguishes between two types of pathways (paradigm and alternate),[7] three types of designations (review clock,

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"liability imposed on private parties who are able to disrupt misconduct by withholding their cooperation from wrongdoers." Reinier H. Kraakman, *Gatekeepers: The Anatomy of a Third-Party Enforcement Strategy*, 2 J.L. ECON. & ORG. 53, 53 (1986). A substantial literature analyzing the role of private sector "gatekeepers" has developed from Professor Kraakman's article. *See, e.g.*, JOHN C. COFFEE, JR., GATEKEEPERS: THE PROFESSIONS AND CORPORATE GOVERNANCE (2006). While the FDA is a gatekeeper in the colloquial sense of the term, it is—as a public agency—not the type of private individual or entity associated with the term "gatekeeper" in the academic legal literature. Nonetheless, the term gatekeeping is used in many important analyses of the FDA's marketing authorization role, particularly outside of the legal academy. *See, e.g.*, DANIEL CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA (2010).

3. *See What Does FDA Regulate?*, U.S. FOOD & DRUG ADMIN. (Jan. 18, 2022), https://www.fda.gov/about-fda/fda-basics/what-does-fda-regulate (providing examples for the areas the FDA regulates and the overlap with other agencies).

4. *See infra* Part I.

5. *See infra* Parts II.A–D.

6. An earlier version of this framework is set out, for pedagogical purposes, in MUCHMORE, *supra* note 2, at 93–139. This Article revises the framework, presents it in a two-level format, and demonstrates that it has substantial analytical value. Parts I, III, and the Conclusion of this Article do not overlap in any way with the casebook. While there is some overlapping language in Part I, the content is substantially revised. Of the figures presented in this Article, only Figure 3 (Pathways), included as Appendix A, is a modification of a figure presented in the casebook. All other figures are original to this Article.

7. The reference to "alternatives" in the title of this Article is to alternatives to the paradigm pathway. These *alternatives* include *alternate* pathways, designations, and means of

application assistance, and market exclusivity), and four means of access before marketing authorization (standard investigational use, expanded access, emergency use, and right-to-try access). This framework makes it possible to step back from the details of each marketing authorization program to view the FDA's marketing authorization activities as a whole.

The FDA's most high-profile activity is its marketing authorization role. It is a role the FDA exercises most prominently with respect to medical products, such as drugs, devices, and biologics.[8] However, the FDA also has a marketing authorization role with respect to other product categories, such as food additives, color additives, and tobacco products.[9] There are other FDA-regulated product categories for which no marketing authorization is required.[10]

The FDA's various marketing authorization activities are typically considered separate and highly specific to each product category.[11] This is

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access before marketing authorization. This is the reason for the difference between the use of the word "alternat*ive*" in the title and the phrase "alternat*e* pathway" in the framework itself. *See infra* Part II.B, and especially Figure 2.

8. *See* MUCHMORE, *supra* note 2, at 97–107 (discussing pathways to market for therapeutic products).

9. *See id.* at 107–13 (discussing pathways to market for non-therapeutic products).

10. *See id.* at 113–14 (discussing product categories for which no marketing authorization is required). Product categories for which the FDA, by statute, has no general marketing authorization role include food, cosmetics, dietary supplements, and radiation-emitting consumer products. The FDA has, by regulation, eliminated any agency marketing authorization role for over-the-counter (OTC) drugs compliant with an OTC drug monograph (a regulation setting out permitted active and inactive ingredient combinations) and for certain low-risk medical devices. The FDA has not sought to exercise any marketing authorization authority over those human cells, tissues, and cellular and tissue-based products (which the agency refers to as HCT/Ps) that are not also subject to regulation as "drugs, biologics, devices, or combination products." *Id.*

This absence of a marketing authorization requirement is itself significant. Regulated parties and the FDA frequently dispute whether particular products are properly placed in no-marketing-authorization categories (such as food, cosmetics, or dietary supplements) or authorization-required categories (commonly food additives, drugs, or combination products). *See, e.g.*, United States v. An Article . . . Sudden Change, 409 F.2d 734, 742 (2d Cir. 1969) (concluding that an anti-wrinkle cream marketed with certain claims was a drug rather than a cosmetic); U.S. Food & Drug Admin., Warning Letter to Lifetech Resources (Apr. 18, 2011), https://www.fdalabelcompliance.com/letters/ucm251951 (warning the company that its eyelash and eyebrow growth products, marketed as cosmetics, were also unapproved drugs).

11. This is particularly apparent in treatises and teaching materials. *See, e.g.*, FOOD AND DRUG LAW AND REGULATION (David G. Adams, Richard M. Cooper, Martin J. Hahn & Jonathan S. Kahan eds., 3d ed. 2015) (presenting each marketing authorization process as a component of a regulatory scheme for an individual product category); A PRACTICAL GUIDE

the first article to present a broad framework for analysis of the FDA's marketing authorization processes across product categories. This framework sheds new light on these activities by highlighting the way a wide range of the FDA's marketing authorization activities are built up from a more limited set of basic parts.[12]

Existing literature has analyzed marketing authorization for many FDA-regulated product categories in detail. The literature is extensive with respect to drugs,[13] biologics,[14] and medical devices.[15] Similar literature exists, but in

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TO FDA'S FOOD AND DRUG REGULATION (Kenneth R. Piña & Wayne L. Pines eds., 5th ed. 2014) (similar); PETER BARTON HUTT, RICHARD A. MERRILL & LEWIS A. GROSSMAN, FOOD AND DRUG LAW (4th ed. 2014) (similar). One casebook, Lars Noah's LAW, MEDICINE, AND MEDICAL TECHNOLOGY: CASES AND MATERIALS (5th ed. 2022), makes some effort to discuss processes across some medical product categories (primarily drugs, biologics, and devices). This includes a chapter devoted to "Development and Testing of Experimental Therapies" and a chapter devoted to "Premarket Approval and Postmarket Surveillance." *Id.* at 187, 291; *see also infra* notes 13–30 and accompanying text (discussing literature on marketing authorization for individual product categories).

12. *See infra* Part II (discussing interchangeable-part lawmaking (IPL)).

13. *See, e.g.*, RICHARD A. EPSTEIN, OVERDOSE: HOW EXCESSIVE GOVERNMENT REGULATION STIFLES PHARMACEUTICAL INNOVATION (2006); SAM PELTZMAN, REGULATION OF PHARMACEUTICAL INNOVATION: THE 1962 AMENDMENTS (1974) (contending that the introduction of drug efficacy regulation harms drug consumers more than it helps them, because of the degree to which efficacy regulation slows the introduction of new, effective drugs). Industry-oriented publications focused on the mechanics of the drug marketing authorization process also exist. *See, e.g.*, BRINGING YOUR PHARMACEUTICAL DRUG TO MARKET (Neil P. Dispirito, Ralph F. Hall & Matthew J. Hill eds., 2015). On the development of the concept of bioequivalence used today in the marketing authorization process for generic drugs, see Daniel Carpenter & Dominique A. Tobbell, *Bioequivalence: The Regulatory Career of a Pharmaceutical Concept*, 85 BULL. HIST. MEDICINE 93 (2011). For an in-depth historical analysis of therapeutic choice in America that addresses, but goes beyond, the FDA's marketing authorization role, see LEWIS A. GROSSMAN, CHOOSE YOUR MEDICINE: FREEDOM OF THERAPEUTIC CHOICE IN AMERICA (2021).

14. *See, e.g.*, Henry Grabowski & Erika Lietzan, *FDA Regulation of Biosimilars*, *in* FDA IN THE 21ST CENTURY: THE CHALLENGES OF REGULATING DRUGS AND NEW TECHNOLOGIES 414 (Holly Fernandez Lynch & I. Glenn Cohen eds., 2015); Jason Kanter & Robin Feldman, *Understanding and Incentivizing Biosimilars*, 64 HASTINGS L.J. 57 (2012); Henry Grabowski, Genia Long & Richard Mortimer, *Implementation of the Biosimilar Pathway: Economic and Policy Issues*, 41 SETON HALL L. REV. 511 (2011).

15. *See, e.g.*, FRED H. DEGNAN, FDA'S CREATIVE APPLICATION OF THE LAW: NOT MERELY A COLLECTION OF WORDS, 113–28 (2d. ed. 2006); James O'Reilly, *"Left to Our Own Devices, What Did We Get Wrong?" The Medical Device Amendments of 1976 as Seen from the Insider's View*, 74 FOOD & DRUG L.J. 110 (2019); Peter Barton Hutt, Richard A. Merrill & Alan M.

less volume, with respect to animal drugs,[16] combination products,[17] and human cells, tissues, and cellular and tissue-based products (HCT/Ps).[18] There is also some work seeking to evaluate the FDA's marketing authorization processes for medical products more generally.[19] Other work has focused on the relationship between the FDA's marketing authorization decisions and state law tort claims,[20] the various expedited pathways

Kirschenbaum, *The Standard of Evidence Required for Premarket Approval Under the Medical Device Amendments of 1976*, 47 FOOD & DRUG L.J. 605 (1992); Benjamin A. Goldberger, *The Evolution of Substantial Equivalence in FDA's Premarket Review of Medical Devices*, 56 FOOD & DRUG L.J. 317 (2001); Jonathan S. Kahan, *Premarket Approval Versus Premarket Notification: Different Routes to the Same Market*, 39 FOOD DRUG COSM. L.J. 510 (1984).

16. *See, e.g.*, Eugene I. Lambert, *The Reformation of Animal Drug Law: The Impact of 1996*, 52 FOOD & DRUG L.J. 277 (1997).

17. *See, e.g.*, George Horvath, *Emergent Regulatory Systems and Their Challenges: The Case of Combination Medical Products*, 94 WASH. L. REV. 1697 (2019) (analyzing marketing authorization process for combination products).

18. Richard A. Merrill, *Human Tissues and Reproductive Cloning: New Technologies Challenge FDA*, 3 HOUS. J. HEALTH L. & POL'Y 1 (2002) (exploring the FDA's initial decision to regulate human tissue neither as a drug nor a device, but instead as a separate product category developed by regulation rather than statute). Today, under a revised regulatory program, the relevant product category is not human tissue but human cells, tissues, and cellular and tissue-based products (HCT/Ps). Some of these HCT/Ps are regulated solely as HCT/Ps, *see* 21 C.F.R. § 1271.10 (2005), but the regulatory structure explicitly contemplates that some HCT/Ps will also be regulated as drugs, devices, biologics, or combination products. *See* Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing, 66 Fed. Reg. 5447, 5456–57 (Jan. 19, 2001).

19. For a review of empirical literature on the costs and benefits of the FDA's regulation of drugs, biologics, and medical devices, see Anup Malani & Tomas J. Philipson, *The Regulation of Medical Products*, *in* THE OXFORD HANDBOOK OF THE ECONOMICS OF THE BIOPHARMACEUTICAL INDUSTRY 2 (Patricia M. Danzon & Sean Nicholson eds., 2012) (seeking "to shed light on whether the policies of the agency itself are safe and effective when measured in terms of economic efficiency"). For a discussion of the FDA's role in marketing authorization for non-therapeutic uses of drugs and devices, see Patricia J. Zettler, *The FDA's Power Over Non-Therapeutic Uses of Drugs and Devices*, 78 WASH. & LEE. L. REV. 379 (2021).

20. For some prominent examples, see Daniel E. Troy, *The Case for FDA Preemption*, *in* FEDERAL PREEMPTION: STATES' POWERS, NATIONAL INTERESTS (Richard A. Epstein & Michael S. Greve eds., 2007); Catherine M. Sharkey, *Field Preemption: Opening the 'Gates of Escape' from Tort Law*, 50 J. LEGAL STUD. S27 (2021); Catherine M. Sharkey, *Inside Agency Preemption*, 110 MICH. L. REV. 521 (2012); Richard A. Epstein, *The Case for Field Preemption of State Laws in Drugs Cases*, 103 NW. U.L. REV. 463 (2009) [hereinafter Epstein, *The Case for Field Preemption*]; Richard A. Epstein, *Why the FDA Must Preempt Tort Litigation: A Critique of* Chevron *Deference and a Response to Richard Nagareda*, 1 J. TORT L. 5 (2006) [hereinafter Epstein, *Why the FDA Must Preempt*]; *see also* George Horvath, *supra* note 17, at 1702 (suggesting that, for medical

available for medical products,[21] the relationship between expedited pathways and the various designations,[22] the relationship between the FDA's

products, FDA marketing authorization decisions and U.S. Supreme Court preemption decisions may operate as an emergent system).

21. *See, e.g.*, GROSSMAN, *supra* note 13, at 162–96 (discussing the role of AIDS activists in pressuring the FDA to develop accelerated approval pathway); Jordan Paradise, *Three Framings of "Faster" at the FDA and the Federal Right to Try*, 11 WAKE FOREST J.L. & POL'Y 53 (2020) (discussing the relationship between previously-established expedited pathways for medical products and the federal Right to Try Act); Thomas J. Hwang & Aaron S. Kesselheim, *Leveraging Novel and Existing Pathways To Approve New Therapeutics to Treat Serious Drug-Resistant Infections*, 42 AM. J.L. & MED. 429 (2016) (analyzing pathways for products to treat drug-resistant infections).

22. *See, e.g.*, Erika Lietzan, *Access Before Evidence and the Price of the FDA's New Drug Authorities*, 53 U. RICH. L. REV. 1243, 1308 (2019) (arguing that the "true cost" of requiring approval for new drugs is the "period of monopoly pricing" associated with new-drug approvals); Erika Lietzan, *The Myths of Data Exclusivity*, 20 LEWIS & CLARK L. REV. 91, 93–103 (2016) (exploring the relationship between data exclusivity periods and the available pathways for both small-molecule drugs and biologics).

There is a particularly extensive body of writing on priority review. While the FDA's priority review process developed in negotiations between industry and the FDA, *see Priority Review*, FOOD & DRUG. ADMIN. (Jan. 4, 2018), https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review, the transferable priority review voucher was the result of congressional implementation of an academic proposal. The original proposal was David B. Ridley, Henry G. Grabowski & Jeffrey L. Moe, *Developing Drugs for Developing Countries*, 25 HEALTH AFFS. 313, 313 (2006); *see also* David Ridley, *Home*, PRIORITY REV. VOUCHERS, https://sites.fuqua.duke.edu/priorityreviewvoucher/ (last visited Aug. 16, 2022) (providing a brief summary of the relationship between the academic proposal and the statute). Professor Ridley and colleagues have continued to publish on the economics of priority review vouchers. *See, e.g.*, David B. Ridley, Pranav Ganapathy & Hannah E. Kettler, *US Tropical Disease Priority Review Vouchers: Lessons in Promoting Drug Development and Access*, 40 HEALTH AFFS. 1243 (2021). This high-profile program has itself generated substantial literature. *See, e.g.*, Oulu Wang, *Buying and Selling Prioritized Regulatory Review: The Market for Priority Review Vouchers as Quasi-Intellectual Property*, 73 FOOD & DRUG. L.J. 383, 383 (2018) (analyzing "the priority review vouchers that have been issued, transferred, and redeemed to date"). A broad theme of this literature is the question of whether the transferable priority review voucher program is effective in achieving its goals.

In support of the program, see, for example, Andrew S. Robertson, *Preserving an Incentive for Global Health R&D: The Priority Review Voucher Secondary Market*, 42 AM. J.L. & MED. 524, 541 (2016), which analyzes the secondary market in priority review vouchers and suggests that there may be diminishing returns to aggressive expansion of the program. For one criticism of the program, see, Jonathan J. Darrow, Michael S. Sinha & Aaron S. Kesselheim, *When Markets Fail: Patents and Infectious Disease Products*, 73 FOOD & DRUG L.J. 361, 375–76 (2018), which questions the efficacy of the priority review voucher program, at least for purposes of incentivizing products for the treatment or prevention of infectious diseases. For another criticism, see Ana Santos

marketing authorization decisions and Center for Medicare and Medicaid Services coverage decisions,[23] the processes for authorizing new uses of already-marketed products,[24] the various means of access to medical products before marketing authorization,[25] and the relationship between marketing authorization pathways for drugs and medical devices.[26] Separately, there is

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Rutschman, *The Priority Review Voucher Program at the FDA: From Neglected Tropical Diseases to the 21st Century Cures Act*, 26 ANNALS HEALTH L. 71, 98 (2017), which suggests that "the efficacy of the program is questionable," and notes several potential harmful effects.

23. *See, e.g.*, GROSSMAN, *supra* note 13, at 257–82 (discussing the ways that coverage decisions by the Center for Medicare and Medicaid Services (CMS) and private insurers impact real-world ability to choose medical treatments); Rachel E. Sachs, *Delinking Reimbursement*, 102 MINN. L. REV. 2307 (2018) (discussing proposals to delink, for drugs, CMS coverage decisions, and FDA marketing authorization decisions); Bruce Patsner, *Marketing Approval Versus Cost of New Medical Technologies in the Era of Comparative Effectiveness: CMS, Not FDA, Will Be The Primary Player*, 3 J. HEALTH & LIFE SCI. L. 38 (2010) (suggesting that for medical products, FDA marketing authorization decisions may soon be overshadowed by CMS coverage decisions).

24. *See, e.g.*, Halabi, *supra* note 2, at 10–11 (suggesting that a "drug repurposing ecosystem" exists and functions quite well, contributing consistently to the development of new uses for existing drugs); Rebecca S. Eisenberg, *The Problem of New Uses*, 5 YALE J. HEALTH POL'Y, L. & ETHICS 717 (2005) (exploring the relationship between patent law, market exclusivity, and trade secrecy in reducing developer incentives to seek approval of new uses for drugs already on the market). On the broader regulatory challenges posed by technologies that may continue to develop after marketing begins, see Rachel E. Sachs, *Regulating Intermediate Technologies*, 37 YALE J. ON REG. 219 (2018).

25. GROSSMAN, *supra* note 13, at 162–200 (discussing the role of AIDS activists in pressuring the FDA to speed access to unapproved drugs); Paradise, *supra* note 21 (discussing the relationship between previously established means of access before marketing authorization and the Federal Right to Try Act).

26. Professor Richard Merrill has compared the "architecture" of the FDA's regulatory process for drugs and medical devices. Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753 (1996). In that article, Professor Merrill traced the development of two models of marketing authorization for FDA-regulated medical products. The first, the "New Drug Approval Model," applies to the regulation of drugs and biologics. *Id.* at 1757–58. Under the new drug model, the FDA must give its affirmative assent at numerous steps throughout the process of developing a new product. *Id.* at 1797–98. If competing priorities or resource constraints delay FDA action, the drug developer must wait to proceed until the agency chooses to assent. *Id.* at 1798.

This contrasts with a separate "Medical Device Model" that applied—at the time—only to medical devices. *Id.* at 1800. Today, a similar model applies to tobacco products as well. *See infra* notes 174–177 and accompanying text. In Professor Merrill's view, both Congress and the FDA deliberately sought to develop a method of medical device regulation that was not based on the new-drug model. Merrill, *supra*, at 1800, 1812, 1821. Instead, they sought to develop "a new type of regulatory statute, one that would assure careful review of the few high-risk

some writing on the marketing authorization processes for food additives[27] and color additives,[28] some discussion of the relationship between categories that require marketing authorization and those that do not,[29] and a growing literature on marketing authorization processes for tobacco-products.[30]

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technologies but permit less intrusive, less costly regulation for most devices." *Id.* at 1808.

For another perspective on the relationship between pathways for drugs and devices, see Horvath, *supra* note 17, at 1727–39, which uses the increasingly prominent combination-product category to explore this relationship.

27. *See, e.g.*, Lars Noah & Richard A. Merrill, *Starting from Scratch?: Reinventing the Food Additive Approval Process*, 78 B.U. L. REV. 329 (1998) (noting delays in the approval of new food additives and proposing various reforms).

28. Writing explicitly focused on color additives is relatively rare. For one recent example, see Brenda Seidman, *The Grays of Medical Device Color Additives*, 69 FOOD & DRUG L.J. 491 (2014). Marketing authorization for color additives is addressed most frequently within more general discussions of carcinogen regulation at the FDA. *See, e.g.*, Richard A. Merrill, *FDA's Implementation of the Delaney Clause: Repudiation of Congressional Choice or Reasoned Adaptation to Scientific Progress?*, 5 YALE J. ON REG. 1, 9–10, 36–48 (1988) (discussing FDA marketing authorization decisions—and related litigation—involving color additives); Margaret Gilhooley, *Plain Meaning, Absurd Results and the Legislative Purpose: The Interpretation of the Delaney Clause*, 40 ADMIN. L. REV. 267, 275–77, 294–96 (1988) (same).

29. Lewis A. Grossman, *Food, Drugs, and Droods: A Historical Consideration of Definitions and Categories in American Food and Drug Law*, 93 CORNELL L. REV. 1091, 1092–94; 1147–48 (2008) (discussing the relationship between food, drugs, and dietary supplements, and suggesting a thought experiment combining all three into a single category, "droods"); Lewis A. Grossman, *FDA and the Rise of the Empowered Consumer*, 66 ADMIN. L. REV. 627 (2014) (discussing rise of social movements reacting to decisions either to decline to grant marketing authorization for, or to remove existing marketing authorization for, certain drugs, food additives, and products that would today qualify as dietary supplements).

30. *See, e.g.*, Eric N. Lindblom, *The Tobacco Control Act's PMTA & MRTP Provisions Mean To Protect the USA from Any New Tobacco Products that Will Not Reduce Health Harms–But FDA Isn't Cooperating*, 23 J. HEALTH CARE L. & POL'Y 121 (2021) (criticizing certain FDA marketing authorization decisions with respect to tobacco products); Desmond Jenson, *Ten Years of FDA Tobacco Regulation: Lessons For Public Health Stakeholders*, 40 J. LEGAL MED. 335, 345–48 (2020) (criticizing the FDA's failure to use its marketing authorization authority more aggressively against e-cigarettes); Eric N. Lindblom, *What is "Appropriate for the Protection of the Public Health" Under the U.S. Tobacco Control Act?*, 74 FOOD & DRUG L.J. 523 (2019) (arguing that the statutory marketing authorization standard for tobacco products requires FDA to exclude consideration of non-health impacts of its marketing authorization decisions); Desmond Jenson, Joelle Lester & Micah L. Berman, *FDA's Misplaced Priorities: Premarket Review Under the Family Smoking Prevention and Tobacco Control Act*, 25 TOBACCO CONTROL 246 (2016) (criticizing numerous aspects of FDA's approach to marketing authorization for tobacco products); *see also* Lars Noah & Barbara A. Noah, *Nicotine Withdrawal: Assessing the FDA's Effort to Regulate Tobacco Products*, 48 ALA. L. REV. 1 (1996) (discussing earlier, unsuccessful FDA effort to regulate cigarettes as combination products).

The framework developed here makes four primary contributions. First, the framework provides a basic terminology based on functional characteristics of the relevant pathways, designations, and means of access before marketing authorization.[31] This functional terminology permits types of cross-category analysis that are otherwise difficult to express. It also emphasizes the distinct role of each aspect of the framework.[32]

Second, the framework suggests that the "paradigms and alternatives" structure that can be seen at the FDA has developed, in part, to manage the tradeoff between Type I and Type II error in the FDA's marketing authorization decisions.[33] The paradigm pathways are focused on reducing the risk of Type I error (which occurs when the FDA permits marketing of a product that should have been kept off the market). The three sets of "alternatives" to the paradigm pathway (alternate pathways, designations, and means of access before marketing authorization) each function in the regulatory program as a means of reducing the risk of Type II error (which occurs when the FDA keeps a product off the market when it should have permitted marketing of the product). They each address different potential causes of Type II error. And they each do this in a manner that largely avoids tinkering with the standard applied in the relevant paradigm pathway.

Third, the framework suggests that there are substantive consequences to assigning particular government functions to one agency rather than another.[34] Cross-category analysis reveals striking similarities in the structure of programs used by the FDA to administer marketing authorization for highly disparate product categories. This suggests that a congressional decision to assign a particular function to the FDA will have consequences both for the way Congress structures the program and the way the Agency implements the program. A similar program assigned to the Federal Trade Commission, the U.S. Department of Agriculture (USDA), or the Environmental Protection Agency is likely to be both structured differently by Congress and implemented differently by the agency to which it is assigned. This has implications for discussions of potential macro-level changes to the FDA's structure. It may also have some value in analyzing the programs of the FDA's foreign counterparts—some of which have very different macro-level structures.

Fourth, the framework highlights a previously overlooked phenomenon that is visible in the historical development of the FDA's marketing authorization programs.[35] This phenomenon, which the Article terms

31. *See infra* Part II.

32. These distinct roles are often blurred in the FDA's public communications. *See infra* note 90.

33. *See infra* Part II.

34. *See infra* Part II.

35. *See infra* Part II.

"interchangeable-part lawmaking" (IPL), occurs when a government takes a portion of its law in one subject area and uses it as a model for its own law in another subject area.[36] It is, in other words, the legal analogue to the interchangeable-part manufacturing process. IPL is strikingly visible (once one begins to look for it) in the statutes administered by the FDA. But it also likely exists in statutes administered by other federal, state, and foreign government agencies. IPL has substantial implications for statutory interpretation, as well as for numerous strands of academic literature. Relevant literature includes recent work on the role of agencies in statutory drafting, on empirical analysis of legislative text, and on path dependence in government institutions.[37]

This Article proceeds as follows. Following this introduction, Part I presents the framework. Part I.A discusses pathways to market and introduces a new distinction between paradigm pathways and alternate pathways. A paradigm pathway requires the FDA to determine that the product meets the most rigorous version of the requirement the applicable statutes and regulations set for marketing authorization. Alternate pathways are processes by which a product can receive marketing authorization without following the paradigm pathway. There is one—and only one—paradigm pathway for each product category subject to marketing authorization. Some product categories have multiple alternate pathways while others have none.

Part I.B presents a related concept currently applicable only to certain medical products: the designations. These are not pathways to market, but methods developed by Congress[38] and the FDA to encourage the development of, and grant of marketing authorization for, favored medical products. This

36. In an excellent study published shortly before this Article went to press, Jennifer Nou and Julian Nyarko address a related phenomenon they term "regulatory diffusion." *See* Jennifer Nou & Julia Nyarko, *Regulatory Diffusion*, 74 STAN. L. REV. 897, 897 (2022) (describing "regulatory diffusion" as occurring "when an agency adopts a substantially similar rule to that of another agency"). Their large-dataset analysis examines situations where federal agencies borrow text from regulations promulgated by other federal agencies. *Id.* From this Article's perspective, regulatory diffusion is one form of IPL. However, there are other forms as well. For example, as Part II.D. demonstrates, Congress has repeatedly used existing programs as interchangeable parts for new programs administered by a single agency, the FDA. In other words, Congress has used existing programs as interchangeable parts in situations that do not involve diffusion.

37. IPL may also provide some perspective on the phenomenon social scientists describe as institutional isomorphism. *See generally* Paul J. DiMaggio & Walter W. Powell, *The Iron Cage Revisited: Institutional Isomorphism and Collective Rationality in Organizational Fields*, 48 AM. SOC. REV. 147 (1983) (setting out the concept); THE NEW INSTITUTIONALISM IN ORGANIZATIONAL ANALYSIS (Paul DiMaggio & Walter W. Powell eds., 1991) (presenting essays analyzing institutional isomorphism in various organizational fields).

38. When discussing statute-making, this Article uses the word "Congress" as shorthand for the process of bicameralism and presentment required by the U.S. Constitution. *See* U.S. CONST. art. I, § 7.

Part groups these designations into three categories for analysis: review clock designations, application assistance designations, and market exclusivity designations. Part I.C discusses four means of access before marketing authorization. The first is standard investigational use, the process used to provide limited access for the research necessary to provide data for the FDA to review. The second is expanded access, a set of programs to provide access to investigational products to those who are not research subjects. The third is emergency use, a process by which the FDA can authorize emergency use of unapproved products in response to declared emergencies. The fourth is right-to-try access, a recent statutory innovation that sets out circumstances under which a drug sponsor may choose—without FDA involvement—to provide an investigational drug, for treatment use, to an individual patient.

Part II sets out four contributions of the framework presented in Part I. Part II.A addresses the concrete benefits of a functional terminology for analysis of the FDA's marketing authorization programs. Part II.B suggests that the "paradigms and alternatives" structure that can be seen at the FDA has developed, in part, to manage the tradeoff between Type I and Type II error in the FDA's marketing authorization decisions. Part II.C suggests that there are substantive consequences to assigning particular government functions to one agency rather than another. Part II.D suggests that IPL provides a useful perspective on the FDA's marketing authorization programs. Then the Article concludes.

I. THE FRAMEWORK

This Part presents a two-level framework for analysis of the FDA's marketing authorization programs.[39] It begins with an overview of five types

39. The framework presented here is one way to organize analysis of the FDA's marketing authorization programs, but it is not the only way. The author thanks Lewis Grossman for suggesting a different approach built around the "mode of review" applicable to each marketing authorization decision. Under such an approach, marketing authorization decisions can be divided into three broad categories: approval, notification, and self-determination. First, there are approval programs where marketing authorization requires an affirmative decision by the FDA to grant such authorization. Second, there are notification programs where marketing authorization can take effect without affirmative FDA action, such as following some specified time period after the FDA receives (and declines to challenge) a notification to the agency. Third, there are situations where marketing is authorized based solely on a regulated entity's self-determination that background regulatory requirements—such as prohibitions on adulteration and misbranding—are satisfied (without any requirement that the FDA be notified in advance). This mode of review approach highlights aspects of the marketing authorization process that are different from those emphasized by the framework presented in this Article. It suggests, in particular, a way of analyzing the interaction between resource constraints, agency priorities,

of marketing authorization standards administered by the FDA. It then presents the framework itself. At the first level, the FDA's marketing authorization programs are composed of pathways, designations, and means of access before marketing authorization.

At a second level, each of these three concepts has several subdivisions. For pathways, there are paradigm pathways and alternate pathways. For designations, there are review clock designations, application assistance designations, and market exclusivity designations. For means of access before marketing authorization, there is standard investigational use, expanded access, emergency use authorization, and right-to-try access.[40]

The framework is summarized in Figure 1, immediately below.

FIGURE 1:

THE FRAMEWORK	
Pathways	Paradigm
	Alternate
Designations	Review clock
	Application assistance
	Market exclusivity
Means of Access Before Marketing Authorization	Standard investigational use
	Expanded access
	Emergency use
	Right to Try access

and the structure of marketing authorization programs. Space constraints prevent further development of these issues here, but they suggest important topics for future work.

40. Some readers have asked about the role of post-market requirements, such as Risk Evaluation and Mitigation Strategies (REMS) and post-approval study requirements, in the framework presented in this Article. The framework presented here conceptualizes post-market requirements as background regulatory requirements that apply to certain products after marketing authorization is granted. They function in a manner similar to background requirements such as establishment-registration requirements and the standard prohibitions on adulteration and misbranding. *See generally* MUCHMORE, *supra* note 2, at 141–63 (discussing background requirements). Some post-market requirements are tied to marketing authorization because they may be required as part of the marketing authorization process. A prominent example is post-approval study requirements for drugs and biologics that receive marketing authorization through accelerated approval. But, under the framework presented here, there does not appear to be a reason to treat these post-approval study requirements in a manner different from other requirements imposed as part of the FDA's marketing authorization decisions.

The FDA requires marketing authorization for drugs, biologics, devices, food additives, color additives, animal drugs, and tobacco products. There are other products subject to FDA jurisdiction for which no marketing authorization is required.[41] At a broad level, it is useful to think of five basic marketing authorization regimes enforced by the FDA.[42] Four of these are marketing authorization standards;[43] the fifth is the absence of a marketing authorization requirement. These regimes are safety only; safety and efficacy; safe, pure, and potent; protection of the public health; and no marketing authorization required. At this broad level, the standard for food and color additives is safety; the standard for drugs and devices is safety and efficacy;[44] the standard for biologics is safety, purity, and potency; and the standard for tobacco products is protection of the public health. No marketing authorization required is the standard for food, dietary supplements, cosmetics, radiation-emitting products, and those HCT/Ps that are not also regulated in another product category.[45]

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41. These include foods, cosmetics, dietary supplements, radiation-emitting products, and those HCT/Ps regulated solely under § 361 of the Public Health Services Act (PHSA), 42 U.S.C. § 264. *See* MUCHMORE, *supra* note 2, at 113–14. Those products are regulated instead under the FDA's post-market authorities, such as prohibitions on adulteration, prohibitions on misbranding, and establishment registration requirements. *See id.* at 141–63.

42. Here, a note on terminology is in order. The FDA uses a variety of terms to describe the processes by which it permits a particular product to be marketed in the United States. These terms have developed over time and are not always used consistently. The FDA is a large organization. Its written materials develop gradually over time, with different officials choosing to emphasize different distinctions between the various marketing authorization processes. For some materials, such as those produced through notice-and-comment rulemaking, the agency cannot easily change them—even to clarify terminology—without undergoing an extensive legal process. Moreover, the fact that some products are regulated in more than one category creates additional terminological complications.

Roughly speaking, however, the FDA's current use of these terms is as follows. Some products are formally approved (new drugs), listed (color additives), or licensed (biologics). These terms denote a finding by the FDA that the relevant product meets the applicable standard of safety and (where applicable) efficacy. Medical devices can be either approved or cleared—with the former reserved for products that undergo a more rigorous review process (premarket approval), and the latter used for products that undergo a less rigorous review process (premarket notification). Tobacco products receive marketing orders. Other products, such as many substances added to food, are permitted on the market based on a determination that they are exempt from the FFDCA's definition of food additive. Some animal drugs are conditionally approved, and some animal drugs are indexed as explicitly unapproved products that are nonetheless permitted to be marketed.

For a recent FDA consumer update discussing the difference between those marketing authorization decisions the FDA considers to be "approval" and those it does not, see *Is It Really 'FDA Approved'?*, U.S. FOOD & DRUG ADMIN. (May 10, 2022),

However, these broad distinctions break down when looking closely at the actual statutory language and implementing regulatory requirements. As set out in more detail in the next section, most product categories involve more than one potential pathway to marketing authorization, with only the paradigm pathway involving a determination that the most rigorous version of the relevant standard is satisfied.[46]

A. Pathways

The first main component of the framework consists of pathways to market. A pathway to market is a process by which the FDA grants marketing authorization. The framework divides pathways to market for FDA-regulated products into two broad sets: *paradigm pathways* and *alternate pathways*. Paradigm pathways are the archetype for the relevant product

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https://www.fda.gov/consumers/consumer-updates/it-really-fda-approved.

43. While there are five basic marketing authorization standards, there are two which operate in a fairly, but not entirely, parallel manner. These are the "safety and efficacy" standard applicable to drugs, and the "safe, pure, and potent" standard applicable to biologics. For a combination of historical and statutory reasons, the FDA regulates biologics both as "drugs" under FFDCA, § 201(g)(1), 21 U.S.C. § 321 and "biological product[s]" under PHSA, § 351(i), 42 U.S.C. § 262(i). *See* MUCHMORE, *supra* note 2, at 97–98. Over time, this has developed into a situation where roughly parallel pathways exist for both drugs and biologics.

44. However, the standard of safety and efficacy required for drugs is higher than the standard of safety and efficacy required for devices. *Compare* FFDCA § 505(d), 21 U.S.C. § 355(d) (requiring safety and "substantial evidence" of efficacy), *with* FFDCA § 515(d)(2), 21 U.S.C. § 360e(d)(2) (requiring only "reasonable assurance" of safety and efficacy).

45. Authorization is required, however, for certain label claims for food and dietary supplements. As these products can be marketed without the specific label claims in question (and many were marketed before label claims for food were allowed, and before dietary supplements were a separate product category), the framework set out in this Article does not treat the label claim authorization process to be a form of marketing authorization. Excluding label claim authorization from the framework is perhaps somewhat arbitrary, as its intended uses—usually set out as label claims—are the core reason many products qualify as "drugs" or "devices," rather than articles that fall outside of FDA jurisdiction. Nonetheless, this Article takes the position that drawing a sharp line between marketing authorization processes (for the product categories addressed in this framework) and claim-authorization processes (for already-marketable food and dietary supplements) captures something important about the FDA role with respect to the products and industries involved. For further discussion of these claims-authorization processes, see *infra* Part II. A chart of these processes is included as Appendix D.

Additionally, the FDA has determined by regulation not to subject a subset of drugs and medical devices to marketing authorization. These are certain OTC drugs and certain low-risk medical devices. *See* MUCHMORE, *supra* note 2, at 114.

46. *See infra* Part I.A.

category. Each paradigm pathway requires a determination by the FDA that the product meets the most rigorous version of the requirement the applicable statutes and regulations set for marketing authorization. However, they are not necessarily the typical pathway used. For some product categories, marketing authorization occurs far more frequently through one or more alternate pathways.

Alternate pathways are processes by which a product can receive marketing authorization without following the paradigm pathway. Most alternate pathways do not formally alter the requirement applicable to the relevant product category. Instead, they permit the requirement to be satisfied in one of five different ways. First, an alternate pathway may permit marketing authorization based on data held by the FDA that the applicant neither owns nor has a right to access.[47] Second, an alternate pathway may permit marketing authorization based on establishing some specified degree of similarity to a product already on the market (through either marketing authorization or grandfathering).[48] Third, an alternate pathway may permit marketing authorization based on some endpoint (roughly speaking, a measurable study target) other than the ultimate clinical outcome in the full population of potential users.[49] Fourth, an alternate pathway may permit marketing authorization by exempting a product from regulation under the seemingly applicable category.[50] Fifth, an alternate pathway may formally alter the marketing authorization standard applicable to the paradigm pathway.[51]

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47. This type of alternate pathway is available for drugs and is known as a § 505(b)(2) application. *See* MUCHMORE, *supra* note 2, at 99.

48. This type of alternate pathway, involving similarity to a product already on the market, is available for generic drugs, generic animal drugs, biosimilar biological products, interchangeable biological products, substantially equivalent medical devices, and substantially equivalent tobacco products. *See id.* at 99–100, 102–03, 112–13.

49. This type of alternate pathway is, of course, only relevant to product categories for which the paradigm pathway requires proof of efficacy in humans. These stand-ins include proof of efficacy at satisfying a surrogate endpoint (an endpoint other than clinical efficacy, but reasonably likely to predict clinical efficacy) in humans, proof of efficacy on some clinical endpoint other than irreversible morbidity or mortality, proof of efficacy in animals, or proof of safety and efficacy (via a favorable risk–benefit ratio) in a limited subpopulation of potential users. *See id.* at 100–01.

50. The first form of this type of alternate pathway, exemption from the product category itself, is available for certain substances added to food. This pathway leads to exemption from the food additive definition. It is used for substances generally recognized as safe (GRAS) and substances in food-contact articles that fall below the threshold of regulation. *See id.* at 109–10. The second form of this type of alternate pathway is available for OTC drugs subject to a monograph and for medical devices exempted from premarket notification requirements. *See id.* at 103–05.

51. Two types of formal alteration in the applicable standard exist. The first is based on the

In addition to products that receive marketing authorization through existing paradigm and alternate pathways, there are also products that received marketing authorization through either a former pathway or a grandfathering provision.[52] "A former pathway is a pathway that once existed but is no longer available."[53] In many cases, some products approved through these former pathways (when they were available) continue to have marketing authorization, even though those former pathways no longer exist.[54]

A grandfathering provision is a statutory or regulatory provision providing that certain existing products can continue to be marketed—despite a significant change in the applicable regulatory regime—unless or until that product's authorization is explicitly revoked by statute or regulation.[55]

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limited size of the product's potential market. This type of formal alteration in the applicable standard is available for medical devices, *see id.* at 106 (describing humanitarian device exemption), and animal drugs, *see id.* at 106–07 (describing conditional approval and indexing). The second type of formal alteration in the applicable standard is based on a congressional decision to deem a subset of products (at this point, only certain medical gases) "to be approved" once they go through a limited certification process administered by the FDA. *See generally* FFDCA § 576, 21 U.S.C. § 60ddd-1 (setting out this alternate pathway); U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: CERTIFICATION PROCESS FOR DESIGNATED MEDICAL GASES (2015) (describing how FDA intends to implement this certification process). For a congressional testimony on the issues that appear to have led to Congress's decision to create this alternate pathway for medical gases, see generally *FDA User Fees 2012: Issues Related to Accelerated Approval, Medical Gas, Antibiotic Development, and Downstream Pharmaceutical Supply Chain: Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*, 112th Cong. 40 (2012) (statement of Rep. Leonard Lance, Member, H. Subcomm. on Health); *id.* at 86–92 (statement of Michael Walsh, speaking on behalf of the Compressed Gas Association). Congress passed the medical-gas provisions of the FFDCA less than four months after hearing this testimony. *See* Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, §§ 111–13, 126 Stat. 993, 1108–12 (2012) (enacting provisions providing for medical gas certification).

52. MUCHMORE, *supra* note 2, at 95.

53. *Id.*

54. "An example is the GRAS *affirmation process* for food additives. This pathway has been replaced by the GRAS *notification process*, but—unless explicitly withdrawn by FDA—individual affirmations made through the former pathway remain valid." *Id.*

55. "Typically, these provisions are structured to be a temporary part of a transition to a new regulatory regime. They generally apply either to products explicitly approved under a prior regulatory regime or to products lawfully marketed in the United States prior to a particular date. Despite their structure as transitional provisions, many products remain on the market under a grandfathering provision for decades. Product categories with important grandfathering provisions still relevant today include food additives (prior-sanctioned substances), medical devices (products on market prior to May 28, 1976), HCT/Ps (human tissue recovered prior to May 25, 2005), and tobacco products (products on market prior to February 15, 2007)." *See id.* at 95.

FDA has at times made efforts to reduce the backlog of unapproved products marketed

For a chart summarizing the pathways to market administered by the FDA, see Appendix A.

B. Designations

The second main component of the framework consists of designations.[56] No designation provides a pathway to marketing authorization.[57] However, for products proceeding via certain marketing authorization pathways, a designation can lead to substantial advantages during or after the marketing authorization process.[58] Each designation applies only to a subset of products in one or more product categories.[59] Currently, designations are available only for certain products in the

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in reliance on these grandfathering provisions. For a recent effort with respect to drugs, see U.S. FOOD & DRUG ADMIN., GUIDANCE FOR FDA STAFF AND INDUSTRY: MARKETED UNAPPROVED DRUGS—COMPLIANCE POLICY GUIDE (2011) (updating 2006 guidance document on the same topic). FDA abandoned this policy in 2020 after determining that the policy had led to shortages and price increases for certain drugs. *See Termination of the Food and Drug Administration's Unapproved Drugs Initiative; Request for Information Regarding Drugs Potentially Generally Recognized as Safe and Effective*, 85 Fed. Reg. 75,331 (Nov. 25, 2020) (announcing the FDA's decision to abandon its Unapproved Drugs Initiative and withdraw the associated guidance document); *see also* Ravi Gupta, Sanket S. Dhruva, Erin R. Fox & Joseph S. Ross, *The FDA Unapproved Drugs Initiative: An Observational Study of the Consequences for Drug Prices and Shortages in the United States*, 23 J. MANAGED CARE & SPECIALTY PHARMACY 1066 (2017) (describing the study highlighted by the FDA in support of its decision to terminate the Unapproved Drugs Initiative).

56. The FFDCA also uses the term "designation" in one manner that is different from the others discussed in this Part. The use is specific to medical gases, a subcategory of drugs limited to certain drugs administered in gaseous form. *See* FFDCA § 575(2); 21 U.S.C. § 360ddd(2). The FFDCA lists seven specific medical gases as "designated medical gases." FFDCA § 575(1); 21 U.S.C. § 360ddd(1). It also permits the Secretary of Health and Human Services to add other medical gases to this list of "designated medical gases" by administrative action. *See id.* This designation is applied by statute or administrative action to a specific product (a medical gas composed of a certain chemical or combination of chemicals), rather than to an application for marketing authorization. It accordingly operates differently than the other designations addressed by this Article, despite the use of the same statutory term. The two primary effects of inclusion on this list of "designated medical gases" are to require marketing authorization for certain medical gases (many of which were previously treated as grandfathered products) and to serve as a trigger for an alternate pathway making such marketing authorization much easier to obtain. *See supra* note 51.

57. MUCHMORE, *supra* note 2, at 115.

58. *Id.* One way to envision designations is as "flags that can be attached to a particular application to have it treated more advantageously by FDA." *Id.*

59. For a chart setting out these designations and the product categories to which they can apply, see *infra* Appendix B.

drug, biologic, device, combination product, and animal drug categories.[60]

The framework presented here divides these designations into three types: review clock designations, application assistance designations, and market-exclusivity designations.[61] The first type, review clock designations, provide for a commitment by the FDA to try to issue a complete response to a marketing authorization request more rapidly than it would for a typical product.[62] The second type, application assistance designations, provide for FDA assistance in navigating the relevant marketing authorization pathway.[63] The third type, market exclusivity designations, provide for an award—a period of market exclusivity for the approved

60. *See infra* Appendix B.

61. *See* MUCHMORE, *supra* note 2, at 115–22 (discussing the three designation types in more detail). This Article treats as designations only those policy mechanisms that are described with the word "designation" in the relevant statutes, regulations, or FDA documents implementing the relevant program. (For an explanation of the reasons this Article does not treat "designated medical gases" as falling within this group of "designations," see *supra* note 56). Accordingly, it omits some mechanisms which operate in a similar manner to those described here. These fall into two groups.

First, there are several exclusivity periods that the FDA does not describe as designations. These include: (1) new drug product exclusivity (which includes both five-year exclusivity for new chemical entities and three-year exclusivity for new clinical investigations), *see generally* 21 C.F.R. § 314.108 (setting out regulations); *see also Small Business Assistance: Frequently Asked Questions for New Drug Product Exclusivity*, U.S. FOOD & DRUG ADMIN. (Feb. 11, 2016), https://www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/small-business-assistance-frequently-asked-questions-new-drug-product-exclusivity, (2) 180-day exclusivity for generic drugs that succeed in challenging the patent for a pioneer drug, *see generally* U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: 180-DAY EXCLUSIVITY WHEN MULTIPLE ANDAS ARE SUBMITTED ON THE SAME DAY 2–3 (2003) (describing the statutory framework for 180-day exclusivity); *see also* Erika Lietzan & Julia Post, *The Law of 180-Day Exclusivity*, 71 FOOD & DRUG L.J. 327 (2016) (providing detailed analysis of past law, current law, and court decisions on 180-day exclusivity), and (3) pediatric exclusivity for testing certain drugs in pediatric populations in response to an FDA request for such studies, *see generally* U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: QUALIFYING FOR PEDIATRIC EXCLUSIVITY UNDER SECTION 505A OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT 2–3 (1999) (providing an overview of the statutory requirements).

Second, several statutory provisions now explicitly provide for the grant of transferrable priority review vouchers for use on a *future* application. *See generally* MUCHMORE, *supra* note 2, at 116 n.35 (citing relevant statutory provisions). Like market exclusivity designations, statutory provisions providing for priority review vouchers offer an award as an incentive for a successful application. But this award takes the form of a highly valuable voucher rather than an exclusivity period. On priority review vouchers more generally, see *supra* note 22.

62. *See* MUCHMORE, *supra* note 2, at 115–16 (discussing review clock designations).

63. *See id.* at 117–19 (discussing application assistance designations but describing them as "review assistance designations").

product—as an incentive for a successful application.[64]

There is currently only one review clock designation: priority review.[65] There are four application assistance designations: fast track, breakthrough therapy, breakthrough device, and regenerative medicine advanced therapy.[66] There are four market-exclusivity designations: orphan drug designation, qualified infectious disease product designation, competitive generic therapy designation, and designated new animal drugs for minor use and minor species.[67]

For a chart summarizing the designations administered by the FDA, see Appendix B.

C. Means of Access Before Marketing Authorization

The third main component of the framework consists of means of access before marketing authorization. These are ways of providing limited access to a product before marketing authorization. The framework presented here divides these means of access before marketing authorization into four types: standard investigational use, expanded access, emergency use, and right-to-try access.[68] The first, standard investigational use,[69] is the traditional process used to permit the research required to obtain the data necessary for requesting that the FDA grant marketing authorization. Standard investigational use is applicable to all product categories requiring marketing authorization. The second, expanded access, provides for patient access to investigational products outside of the research context. This process, often described as compassionate use, applies to drugs (including biologic drugs) and medical devices.[70] The third, emergency use, is available in declared

64. *See id.* at 119–22 (discussing market exclusivity designations).

65. *See id.* at 115–16 (discussing priority review).

66. *See id.* at 117–19 (discussing application assistance designations but describing them as "review assistance designations").

67. *See id.* at 119–22 (discussing orphan drug designation, qualified infectious disease product (QIDP) designation, and competitive generic therapy (CGT) designation). QIDP designation also includes review clock and application assistance elements, *see id.* at 121, CGT designation also includes some application assistance elements, *see id.* at 121–22. On designated new animal drugs for minor use and minor species, see generally Designation of New Animal Drugs for Minor Uses and Minor Species, 72 Fed. Reg. 41,010, 41,010–11 (July 26, 2007), which promulgates regulations mandated by FFDCA § 573, 21 U.S.C. § 360ccc-2, and codifies those regulations at 21 C.F.R. pt. 516(B) (2021).

68. Each is discussed in more detail in MUCHMORE, *supra* note 2, at 125–39.

69. *Id.* at 125.

70. *See id.* at 131–33.

emergencies.[71] Such emergencies can include both natural events and chemical, biological, or nuclear attacks.[72] Emergency use applies to drugs (including biologic drugs), animal drugs, and medical devices.[73] The fourth, right-to-try access, permits drug sponsors to provide investigational drugs directly to patients, for treatment use, in certain limited circumstances. It applies only to drugs (including biologic drugs).[74]

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71. Emergency use has played a central role in the FDA's response to the COVID-19 pandemic. Most prominently, the FDA has now approved several vaccines for emergency use. Two of those vaccines have since received a biologics license through the appropriate paradigm pathway. *See* Press Release, FDA, Coronavirus (COVID-19) Update: FDA Takes Key Action by Approving Second COVID-19 Vaccine (Jan. 31, 2022), https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-takes-key-action-approving-second-covid-19-vaccine. The FDA has also authorized emergency use of numerous other drugs and devices, ranging from tests to therapeutics. Some of these have been low profile, others have generated national headlines. For a thoughtful summary, see generally NAT'L ACAD. OF SCI., ENG'G, & MED., THE FOOD AND DRUG ADMIN.'S EMERGENCY USE AUTHORIZATION: LESSONS LEARNED FROM THE PAST TO GUIDE THE FUTURE: PROCEEDINGS OF A WORKSHOP IN BRIEF (2021); and Efthimios Parasidis, Micah L. Berman & Patrica J. Zettler, *Assessing COVID-19 Emergency Use Authorizations*, 76 FOOD & DRUG L.J. 441 (2021), which assesses the COVID-19 emergency use authorizations (EUAs) issued between February 4, 2020, and March 8, 2021.

There is not space in this Article to address the important question of whether the FDA's issuance of EUAs at a broad level during the COVID-19 pandemic will result in a future relaxation of the FDA's existing marketing authorization standards. Activist pressure to do so seems highly likely. Whether such efforts will be successful, and the form such success would take, are hard to predict. In the language of this Article, one possible outcome would be the development of one or more alternate pathways modeled on the standards actually applied by the FDA in its major EUA decisions. (As the agency was careful to document, the FDA chose to apply standards substantially higher than required by the relevant statutory language to some of these EUAs. *See* U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: EMERGENCY USE AUTHORIZATION FOR VACCINES TO PREVENT COVID-19, at 3–4 (Oct. 2020)).

72. *See* MUCHMORE, *supra* note 2, at 133–34.

73. *See id.* at 133–38.

74. *See* FFDCA § 561B, 21 U.S.C. § 360bbb-0a; *Right to Try*, U.S. FOOD & DRUG, https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/right-try (last visited Aug. 16, 2022). Right to try access differs from expanded access in several ways. Many of these come from the different statutory provisions on which the two programs are based. *Compare* FFDCA § 561, 21 U.S.C. § 360bbb (expanded access), *with* FFDCA § 561B, 21 U.S.C. § 360bbb-0a (right to try access). The most significant is that right to try access bypasses the FDA entirely. The agency has no role in the sponsor's decision to grant or deny access to a particular patient. *See Right to Try*, *supra* ("FDA does not review or approve requests for Right to Try Act use. FDA's role is limited to receipt and posting of certain information submitted under the Right to Try Act."); *see also* GROSSMAN, *supra* note

For a chart summarizing the means of access to FDA-regulated products before marketing authorization, see Appendix C.

II. CONTRIBUTIONS

The framework set forth here makes four primary contributions. First, it provides a basic terminology based on functional characteristics of the relevant pathways and designations.[75] Second, it suggests that the "paradigms and alternatives" structure that can be observed at the FDA has developed, in part, to manage the tradeoff between Type I and Type II error in the FDA's marketing authorization decisions.[76] Third, it suggests that there are substantive consequences to assigning particular government functions to one agency rather than another.[77] Fourth, it highlights the role of a newly identified phenomenon, IPL, in the FDA's marketing authorization programs.[78] These four contributions are each discussed in more detail below.

For each contribution, the discussion below is necessarily a rough sketch suggesting possibilities for future work.[79] The intent is to demonstrate the value of the framework as a foundation for future analysis.

13, at 198 (highlighting absence of an FDA role in right to try access decisions as a "stark contrast" with the FDA's expanded access program); PARADISE, *supra* note 21, at 64–66 (discussing differences between expanded access and right to try access).

75. *See infra* Part II.A.

76. *See infra* Part II.B.

77. *See infra* Part II.C.

78. *See infra* Part II.D.

79. Full development of the implications sketched in Parts II.B through II.D would require space beyond that available in this Article.

In Part II.B, this Article does not claim that the "paradigms and alternatives" structure was a conscious design choice tied to Type I and Type II error. Instead, it limits its claim to suggesting that the "paradigms and alternatives" structure provides a plausible functional explanation for important aspects of existing marketing authorization programs. In particular, it provides a plausible explanation for why paradigm pathways have remained largely untouched once established, despite intense legislative innovation with respect to the various alternatives to the paradigm pathways (alternate pathways, designations, and means of access before marketing authorization).

In Part II.C, this Article does not claim to establish either that programs located within a single agency will always influence each other, or that such influence has taken place within the FDA. Instead, it suggests that striking similarities between FDA programs for highly disparate product categories make such influence seem plausible within the FDA itself. If such influence does occur within the FDA, that suggests a similar effect is possible within other agencies as well.

In Part II.D, this Article does not claim to establish that Congress, the FDA, or individual decisionmakers within either entity, intentionally uses parts of existing programs as "interchangeable parts" in developing other programs. Establishing such a claim would

A. Functional Terminology

The framework's first contribution is a functional terminology for analysis of the FDA's marketing authorization programs. In legal analysis, it is not unusual for terminological developments to drive both scholarship and court decisions. Prominent examples include the distinction between general jurisdiction and specific jurisdiction;[80] the distinction between property rules, liability rules, and inalienability;[81] and the distinction between rules and standards.[82] Those distinctions demonstrate the value of terminological

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involve legislative history research far beyond what this Article could present. However, this Article takes the position that: (1) the similarities that exist between marketing authorization programs for disparate product categories are striking and go far beyond what could be explained by chance; (2) IPL is a highly plausible explanation for such similarities; and (3) that more detailed future analysis will reveal that IPL does in fact take place.

80. *See* Arthur T. von Mehren & Donald T. Trautman, *Jurisdiction to Adjudicate: A Suggested Analysis*, 79 HARV. L. REV. 1121 (1966). In 1966, Professors von Mehren and Trautman proposed a new terminology for analysis of personal jurisdiction. *See id.* at 1164–66. Civil Procedure professors have used a version of this terminology to teach personal jurisdiction for decades, and the article has repeatedly been cited by the U.S. Supreme Court in leading personal jurisdiction cases. *See, e.g.*, Daimler AG v. Bauman, 571 U.S. 117, 127 (2014); J. McIntyre Machinery, Ltd. v. Nicastro, 564 U.S. 873, 899, 910 (2011) (Ginsburg, J., dissenting); Goodyear Dunlop Tires Operations, S.A. v. Brown, 564 U.S. 915, 919 (2011); Asahi Metal Industry Co. v. Superior Court of California, Solano County, 480 U.S. 102, 117 n.1 (1987) (Brennan, J., concurring in part and concurring in judgment); Helicopteros Nacionales de Colombia, S.A. v. Hall, 466 U.S. 408, 414 nn.8–9 (1984); *id.* at 427 n.5 (Brennan, J., dissenting); Shaffer v. Heitner, 433 U.S. 186, 205 (1977). In 2011, a former Civil Procedure professor, writing for the Court, formally adopted the distinction between general and specific jurisdiction as part of U.S. Supreme Court jurisprudence. *Goodyear*, 564 U.S. at 919 (Ginsburg, J.).

81. *See* Guido Calabresi & A. Douglas Melamed, *Property Rules, Liability Rules, and Inalienability: One View of the Cathedral*, 85 HARV. L. REV. 1089 (1972). In 1972, Professor Guido Calabresi and A. Douglas Melamed proposed a distinction between "property rules," "liability rules," and "inalienability" to describe a set of legal relationships found in both property law and tort law. *Id.* at 1089, 1092–93. The article was a foundational work in the early law and economics movement, and its insights helped to generate a large body of related scholarship. The article was sufficiently influential for the Yale Law Journal to publish a symposium on the 25th anniversary of its publication. *See generally Symposium*, *Property Rules, Liability Rules, and Inalienability: A Twenty-Five Year Retrospective*, 106 YALE L.J. 2081, 2081–2213 (1997).

82. *See* Duncan Kennedy, *Form and Substance in Private Law Adjudication*, 89 HARV. L. REV. 1685 (1976). That article itself is considered one of the foundational works in the critical legal studies movement. *See* MARK KELMAN, A GUIDE TO CRITICAL LEGAL STUDIES 15 (1987). However, the rule–standard distinction it popularized has been fruitful far beyond the limits of critical legal studies. Leading figures in the law an economics movement have analyzed the rule–standard distinction. *See, e.g.*, Isaac Ehrlich & Richard A. Posner, *An Economic Analysis of Legal Rulemaking*, 3 J.

innovation for legal analysis. Scholars working in related academic disciplines have made similar observations on the value of functional terminology.[83]

The framework presented here is based, in part, on terms already used by the FDA—pathway and designation. Its terminological innovations are to distinguish between paradigm pathways and alternate pathways and to distinguish between review clock, application assistance, and market exclusivity designations. This Article also emphasizes the sharp distinction between pathways and designations that the FDA's written materials often obscures.[84]

Based on these terminological innovations, this Article has proposed a two-level framework for analysis of marketing authorization programs at the FDA.[85] Viewing the FDA's marketing authorization programs through this framework provides a foundation for deeper analysis.[86] Without such a framework, the programs easily become a complex set of product-specific programs that discourage engagement by nonspecialists. This complexity can insulate them from critical analysis.

Under this framework, several modes of analysis become apparent. Within product categories, analysts can compare usage rates and outcomes between paradigm pathways and alternate pathways. For those pathways for which designations exists, this comparison can include various combinations of applicable designations. For example, this suggests a way

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LEGAL STUD. 257, 257 (1974) (using the rule–standard framework to conduct an economic analysis of the level of "precision or specificity" of legal requirements); Louis Kaplow, *Rules Versus Standards: An Economic Analysis*, 42 DUKE L.J. 557, 621–22 (1992) (positing that the difference between rules and standards rests entirely on the difference between *ex post* and *ex ante* application of law, and presenting an economic analysis of when each is desirable from the perspective of overall social welfare). Rules and standards are now the subject of a large, diverse body of legal scholarship. *See generally* Adam I. Muchmore, *Uncertainty, Complexity, and Regulatory Design*, 53 HOUS. L. REV. 1321, 1330–32 (2016) (discussing this literature and citing prominent examples).

83. *See, e.g.*, James Mahoney, *Knowledge Accumulation in Comparative Historical Research*, *in* COMPARATIVE HISTORICAL ANALYSIS IN THE SOCIAL SCIENCES 131, 134 (James Mahoney & Dietrich Rueschemeyer eds., 2003) [hereinafter COMPARATIVE HISTORICAL ANALYSIS] (noting value of "well specified concepts" and "typologies," as "[t]hese classification apparatuses enable analysts to formulate new and useful knowledge that is systematically related to and dependent on prior knowledge"); Dietrich Rueschemeyer, *Can One or a Few Cases Yield Theoretical Gains?*, *in* COMPARATIVE HISTORICAL ANALYSIS, *supra*, at 305, 328 (discussing role of "*conceptual equivalencies* across political, social, and cultural boundaries" and "highly *focused theoretical frameworks*" in providing a foundation, and organizing principle, for further academic work).

84. *See infra* note 90 and accompanying text.

85. *See supra* Part I setting out this framework in detail).

86. On the importance of shared terminology for analysis across different academic disciplines, and across methodological "tribe[s]" within disciplines, see PAUL PIERSON, POLITICS IN TIME 7–8 (2004) (citing COMPARATIVE HISTORICAL ANALYSIS, *supra* note 83).

of organizing analysis of each product category.[87] These same types of analysis can be done across different product categories.

In terms of policy, the payoff for such analyses should become clear when it comes time for Congress, the FDA, and relevant stakeholders to update the FDA's regulatory programs. Such conversations occur regularly, as the automatic sunset provisions within the FDA's user fee programs tend to require renegotiation every five years.[88] Moreover, when considering how to regulate new technologies, articulating the possibilities in terms of this framework can clarify the range of possible options.

A similar analysis could potentially be conducted between the FDA and other federal agencies, or between the FDA and its foreign counterparts. In *The Old-New Division in Risk Regulation*, Peter Huber distinguished between two "[s]tatutory [m]odels" for risk regulation—"screening" for new risks and "standard-setting" for old risks.[89] The FDA has both screening and standard-setting functions, but its marketing authorization functions fall primarily into Huber's screening category. It is possible that other agencies with a screening function may have a similar structure of paradigm and alternate pathways or may use some combination of pathways and designations. These could be other federal agencies with product-approval responsibilities. A similar structure could also exist in agencies in foreign countries—either the FDA's foreign counterparts or other foreign agencies with product-approval responsibilities. This Article does not take a position on whether such parallel structures exist. If they do, comparison with the FDA's programs could be fruitful. If they do not, and the FDA's marketing authorization structure turns out to be idiosyncratic, that itself would justify further research into how this approach developed, and why it persists.

This framework's value does not depend on adoption by the FDA. However, the Agency may find this framework useful. One of the FDA's

87. This could include traditional legal analysis (including analysis of the relationship between the role of statutes, regulations, and guidance in each pathway) or various types of empirical analysis. Quantitative empirical analysis might be appropriate for large-volume pathways, such as new drug applications, abbreviated new drug applications, premarket approval of medical devices, and the 510(k) pathway. Some significant empirical work in these areas already exists, and this Article's framework could perhaps provide an organizing principle for meta-analysis of this existing work. Qualitative empirical analysis might be more appropriate for lower volume pathways, such as the Animal Rule for human drugs, conditional approval for animal drugs, and indexing of unapproved animal drugs.

88. These user fee programs now fund such a large portion of the FDA's marketing authorization programs that they are widely considered must-pass legislation. Failing to renew one of these programs would result in sudden, massive layoffs of FDA reviewers funded by the relevant user fees—and would create a bottleneck in the relevant set of marketing authorization programs.

89. Peter Huber, *The Old-New Division in Risk Regulation*, 69 VA. L. REV. 1025, 1030–31 (1983).

major challenges is effective communication with its stakeholders. The breadth of the FDA's regulatory mandate means its stakeholders are broadly distributed and heterogeneous. These include consumers, groups from widely different industries, academic researchers, Congress, other executive agencies, state and local governments, and its foreign counterparts. Moreover, many of the FDA's regulatory decisions turn on a combination of scientific, technical, and regulatory expertise that is rarely united in a single individual.

In its communicative efforts, the FDA relies on a combination of rulemaking, guidance, compliance guides for specific stakeholders (such as small businesses), website explanations, speeches, and webinars. At times, however, these efforts blur distinctions that are apparent when presented under the framework set out in this Article.[90] The FDA might find that the framework presented here makes it easier for the Agency to communicate with its stakeholders.

B. Type I and Type II Error

The framework's second contribution relates to the core goal of the FDA's marketing authorization programs. At a basic level, these programs developed to manage the tradeoff between Type I and Type II error in marketing authorization decisions. As in other situations of decisionmaking under uncertainty,[91] marketing authorization decisions

90. For example, in May 2014, the FDA issued a guidance document seeking to explain its various expedited programs. *See* U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: EXPEDITED PROGRAMS FOR SERIOUS CONDITIONS – DRUGS AND BIOLOGICS (2014) (setting out what remains the FDA's most current guidance on this topic). This document presents accelerated approval (a pathway) sandwiched between two application assistance designations (fast track and breakthrough therapy) and one review clock designation (priority review). *Id.* at 7–8. The result is a document that requires substantial effort and background knowledge to decode. At other times, the FDA has been more careful to explain that a designation is not a pathway to market. *See* U.S. FOOD & DRUG ADMIN., DRAFT GUIDANCE FOR INDUSTRY: SPECIAL CONSIDERATIONS, INCENTIVES, AND PROGRAMS TO SUPPORT THE APPROVAL OF NEW ANIMAL DRUGS FOR MINOR USES AND FOR MINOR SPECIES 15 (2020). The framework presented in this Article, however, might make such explanations both easier for the FDA to convey and easier for stakeholders to understand.

91. As Richard Epstein has argued, the FDA's marketing authorization decisions involve decisionmaking under conditions of uncertainty. EPSTEIN, *supra* note 13; *see also* Richard A. Epstein, *Against Permititis: Why Voluntary Organizations Should Regulate the Use of Cancer Drugs*, 94 MINN. L. REV. 1, 9 (2009); Epstein, *Why the FDA Must Preempt*, *supra* note 20, at 5; Epstein, *The Case for Field Preemption*, *supra* note 20, at 469. It is not realistically possible for the Agency to acquire all the information it would like to have before making marketing authorization decisions. Humans respond heterogeneously to many medical products, so it is not possible to extrapolate precisely from a study in a smaller group to the broader population of potential

involve two types of potential error.[92] Type I error results when the FDA authorizes marketing of a product that it should have kept off the market.[93] Type II error results when the FDA keeps a product off the market when it should have granted marketing authorization.[94]

Those designing regulatory programs will seek, to the extent possible, to minimize both Type I and Type II error. However, in real-world regulatory programs, there is likely to be some degree of tradeoff between the two. Efforts to minimize Type I error are likely to increase the risk of Type II error, while efforts to minimize Type II error are likely to increase the risk of Type I error.

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users. (This is the case even if trials could accurately mimic conditions of actual use—which few would contend they can.) To obtain all relevant information, the Agency would need to observe the product in use, over the long term, in the full population of potential users. This, however, would approximate the patterns of usage that would result from marketing authorization itself. Whether they would in fact match marketing authorization usage patterns would depend in part on whether pricing and public confidence matched the situation that would exist after marketing authorization. Accordingly, it would not be a sensible thing for the FDA to require before granting marketing authorization.

92. Type I and Type II error statistical concepts used to describe the likelihood of a test rejecting a null hypothesis. *See* Lee Kennedy-Shaffer, *When the Alpha Is the Omega:* P-*Values, "Substantial Evidence," and the 0.05 Standard at FDA*, 72 FOOD & DRUG L.J. 595, 602 (2017) ("A Type I error occurs when the test rejects the null hypothesis despite the null hypothesis being true. A Type II error occurs when the test accepts the null hypothesis despite the null hypothesis being false."). They have since come to be used, in somewhat modified form, in academic writing about FDA drug approval decisions. In this context, the FDA makes a Type I error when it authorizes marketing of a drug that it should have kept off the market, and it makes a Type II error when it fails to approve a drug that should be on the market. *See, e.g.*, EPSTEIN, *supra* note 13 (using the terms in this sense); Henry Grabowski & Y. Richard Wang, *Do Faster Food and Drug Administration Drug Reviews Adversely Affect Patient Safety? An Analysis of the 1992 Prescription Drug User Fee Act*, 51 J.L. & ECON. 377, 379 (2008) (similar); Mary K. Olson, *Pharmaceutical Policy Change and the Safety of New Drugs*, 45 J.L. & ECON. 615, 618 (2002) (similar). This usage goes beyond the statistical sense of these error types, as those applying them to FDA typically use an *ex post* evaluation of adverse events as a proxy for Type I error. It is nonetheless a useful way to frame an evaluation of the Agency's marketing authorization decisions. While these error types are most frequently applied to the drug and biologic approval processes, they can also be used with respect to other FDA marketing authorization processes.

93. *See supra* note 92.

94. *Id.*

The framework described above sets out a "paradigms and alternatives" structure that can be seen in the FDA's marketing authorization programs.[95] This structure is based on a combination of paradigm pathways and alternatives to those paradigm pathways. The paradigm pathways developed to protect against Type I error, while the various alternatives to the paradigm pathway developed to protect against Type II error.[96] These alternatives can take the form of alternate pathways, designations,[97] and means of access before marketing authorization. These three sets of alternatives each provide a different way of reducing the risk of Type II error. Figure 2, immediately below, summarizes this "paradigms and alternatives" structure.

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95. On the distinction between this Article's use of "alternatives" and "alternate pathways," see *supra* note 7.

96. These efforts to reduce Type II error can also be approached from the perspective of innovation policy. From this perspective, the focus is not the marketing authorization decision itself. It is, instead, on the downstream effects of the marketing authorization process on resource allocation decisions made by individuals and companies. In terms of innovation policy, some alternatives to the paradigm pathway will increase the expected value of investments in relevant product categories. They do this in various ways. These include: (1) making it more likely that a product will receive marketing authorization; (2) reducing the amount of time or resources necessary to obtain marketing authorization; and (3) increasing the value of a marketing authorization decision through some type of exclusive marketing period. For example, many alternate pathways and review assistance designations may both increase the likelihood that a product will receive marketing authorization and reduce the amount of time or resources necessary to a successful application. Review clock designations will, on average, result in decisions that are made more quickly than for standard applications. As demonstrated by vaccines, therapeutics, and tests during the COVID-19 pandemic, emergency use authorization can at times be a viable route to large-scale (though temporary) marketing. And market exclusivity designations are designed to provide a financially valuable period of exclusive marketing.

For other alternatives to the paradigm pathways, the downstream effects on innovation policy seem less significant. While FDA sometimes permits companies to charge for standard investigational use or expanded access, the amounts that can be charged—and the circumstances in which such charges can be made—are limited. *See, e.g.*, 21 C.F.R. § 312.8(a)–(b) (setting out criteria under which a sponsor may charge for standard investigational use of drugs); 21 C.F.R. § 312.8(a), (c) (setting out criteria under which a sponsor may charge for expanded access to drugs); *id.* § 312.8(d) (limiting the amount that can be charged for a drug provided through either standard investigational use or expanded access); 21 C.F.R. § 812.20(b)(8) (requiring explanation for any circumstance in which a device is to be sold as part of standard investigational use, including "the amount to be charged and an explanation of why sale does not constitute commercialization of the device"); 21 C.F.R. § 812.36 (limiting the amount for which a device provided through expanded access can be sold to a "price . . . based on manufacturing and handling costs only"). The Right to Try Act

FIGURE 2:

THE "PARADIGMS AND ALTERNATIVES" STRUCTURE	
Paradigms (protect against Type I error)	Paradigm pathways
Alternatives (protect against Type II error)	Alternate pathways
	Review clock designations
	Application assistance designations
	Market exclusivity designations
	Standard investigational use
	Expanded access
	Emergency use
	Right to try

The paradigms (the various paradigm pathways) protect against Type I error by requiring compliance with the most rigorous version of the relevant marketing authorization standard. The alternatives (alternate pathways, designations, and means of access before marketing authorization) protect against Type II error in different ways.

Alternate pathways protect against Type II error by permitting marketing authorization without meeting the most rigorous version of the applicable

incorporates the investigational drug charging limits by reference. *See* FFDCA § 561B(b), 21 U.S.C. § 360bbb-0a(b) (requiring that, to be eligible under the right to try act, an investigational drug must be "in compliance with the applicable requirements set forth in section[] . . . 312.8(d)(1) of title 21, Code of Federal Regulations"). A charging limit also exists for one alternate pathway, the humanitarian device exemption (HDE). *See* FFDCA § 520(m)(3); 21 U.S.C. § 360j(m)(3) (providing that, with certain exceptions, devices authorized under the HDE pathway may not be sold "for an amount that exceeds the costs of research and development, fabrication, and distribution of the device"). At the margin, the limited charges permitted in these situations may provide some stimulus to innovation, as they could partially defray some costs of product development. But these are likely to be less significant, as a matter of innovation policy, than those alternatives the paradigm pathway that are not subject to such charging limits.

These alternatives to the paradigm pathway are only one part of the set of innovation policies Congress has included in the FFDCA. For discussion of some other important FFDCA innovation policy provisions, see *supra* note 61.

97. Designations are not themselves pathways to market, and they are at times used with a paradigm pathway, rather than as an alternative to it. However, it is still useful to speak of them as alternatives to the paradigm pathway, as they are alternatives to the pathway in its unmodified form.

marketing authorization standard.[98] Overall, the less rigorous requirements associated with alternate pathways should affect both the number of applications received and the approval rates for applications received. This is a straightforward application of positive economics. All other things being equal, a marketing authorization standard that is less costly to satisfy should result in two things. First, it should result in regulated parties filing more applications. Second, it should result in the FDA granting a larger proportion of the applications it receives.

The three types of designations help protect against the risk of Type II error in different ways. Review clock designations encourage the FDA to focus review resources on particular, favored applications.[99] Application assistance designations encourage the FDA to provide active assistance for favored applications.[100] Market exclusivity designations encourage applications by changing the cost–benefit calculation of potential applicants.[101]

Finally, means of access before marketing authorization reduce the risk of Type II error by providing for availability, in limited circumstances, of products that have not made it through either a paradigm pathway or an alternate pathway.[102]

There may be a simple justification for this approach to balancing the risks of Type I and Type II error. Those involved in designing marketing authorization processes will themselves be operating under conditions of uncertainty.[103] The participants in this process will rarely be able to predict with confidence the results of any change to a particular marketing authorization program.[104] In this situation, there is a clear advantage to a

98. If paradigm pathways were the only pathways to exist, fewer products would receive marketing authorization. Developing the data necessary to satisfy paradigm pathways would not be cost-justified for many products that have been authorized through alternate pathways.

99. *See supra* Part I.B (discussing review clock designations).

100. *See supra* Part I.B (discussing application assistance designations).

101. *See supra* Part I.B (discussing market exclusivity designations).

102. *See supra* Part I.B. Like most efforts to protect against Type II error, their byproduct is some increase in the risk of Type I error. However, the means of access before marketing authorization have some characteristics that minimize the potential harm from that increase in the risk of Type I error. Means of access before marketing authorization do this by minimizing one or more of the following: the number of users who get access before marketing authorization; the circumstances in which that access is provided; and the time period for which that access is provided.

103. At a minimum, this group likely includes politicians, civil servants, lobbyists, and congressional staffers. On the role of uncertainty in regulatory design, see generally Muchmore, *supra* note 82.

104. In particular, they may be concerned that an effort to reduce Type II error will go too far, directly resulting in an excessive increase in Type I error.

program structured as an alternate pathway, designation, or means of access before marketing authorization. If unsatisfactory, such a program can simply be eliminated, returning the relevant marketing authorization program to something close to the status quo before the change. This is likely to be both easier to administer, and easier to accomplish politically, than reversing a substantive change to the standards of the relevant paradigm pathway.[105]

Further support for this suggestion can be found in the separate, claims-authorization processes for food and dietary supplements. As noted earlier, neither food nor dietary supplements are subject to marketing authorization requirements. However, some label claims for both sets of products are subject to claims-authorization requirements.[106] These are health claims based on significant scientific agreement (SSA health claims), qualified health claims, and nutrient content claims.[107] Statutory provisions relating to each of these are found in the Federal Food, Drug, and Cosmetic Act's (FFDCA's) misbranding provisions, and the FDA authorizes them if it finds them to be truthful and not misleading.[108] For a chart summarizing the FDA-administered claims-authorization processes for food and dietary supplements, see Appendix D.

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105. On the possibility that agencies frequently approach statutory drafting as if they were working with a set of interchangeable parts, which could each be added or removed, see *supra* Part II.B.

106. *See generally* MUCHMORE, *supra* note 2, at 271–301 (discussing label claims for food and dietary supplements).

107. The FDA recognizes five primary types of label claims for food and dietary supplements. MUCHMORE, *supra* note 2, at 274–77. These are the four types of claims listed above—for which authorization is required—plus structure/function claims. *Id.* In certain circumstances, dietary supplements can also claim a benefit relating to a classical nutrient deficiency disease. *Id.*

The requirements for structure/function claims depend on whether the product is a conventional food or a dietary supplement. *Id.* For conventional food, FDA has no role in reviewing a structure/function claim before it is made. *Id.* For a dietary supplement, 21 C.F.R. § 101.93 requires that the "manufacturer, packer, or distributor" notify the FDA "[n]o later than 30 days" after the first day on which a supplement making such a claim is first marketed. 21 C.F.R. § 101.93(a)(1).

108. *See generally* FFDCA § 403(r), 21 U.S.C. § 343(r). For health claims based on significant scientific agreement (SSA health claims), the FDA requires significant scientific agreement before it will conclude that the claim is truthful and not misleading. *See* 21 C.F.R. pt. 101, Subpart E (setting out requirements for SSA health claims). After several losses in court, *see* Pearson v. Shalala, 164 F.3d 650 (D.C. Cir. 1999); Whitaker v. Thompson, 248 F. Supp. 2d 1 (D.D.C. 2002), the FDA developed a separate procedure under which it would exercise enforcement discretion for claims that did not meet the SSA standard, but were nonetheless truthful and not misleading. *See* U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: FDA'S IMPLEMENTATION OF QUALIFIED HEALTH CLAIMS (2006); U.S. FOOD &

For each of these, the FDA administers only a single claims-authorization process—there are no alternate processes available and no system of designations. Moreover, means of access before marketing authorization are unnecessary because these products are already available—they are not subject to any marketing authorization requirement. This is a striking difference between these claims-authorization processes and the marketing authorization processes discussed earlier. There are no alternatives to the single available claims-authorization process for any specific product-claim combination.

One plausible explanation for this difference is that Type II error is far less of a concern for claims-authorization processes than for marketing authorization processes. At the product level, Type II error does not exist—no product is kept off the market because of the agency's failure to authorize a claim. At the claim level, Type II error simply results in a failure to add a particular claim to the product label. This is a far less severe error than a failure to make a product available. Those who are confident the FDA was wrong can simply buy the product without the claim.

Examining these claims-authorization processes next to the marketing authorization process addressed in Part I provides additional support for the theory set out in this section. To recap, the "paradigms and alternatives" structure seen in the FDA's marketing authorization processes plausibly developed as a way to manage the tradeoff between Type I and Type II error. Paradigm pathways developed to protect against Type I error, while the three sets of alternatives to the paradigm pathways developed to protect against Type II error. No such structure is necessary for claims-authorization processes, as Type II error presents far less cause for concern when the product itself does not require marketing authorization.

C. The Organization of Government

The framework's third contribution is to suggest that there are substantive consequences to assigning particular government functions to one agency rather than another. As noted earlier, this is the first Article to examine the FDA's marketing authorization processes as a whole. This is distinct from more traditional efforts to analyze individual regulatory programs or small groups of related programs.[109] Cross-category analysis suggest that looking at all marketing authorization programs administered by a single agency can provide a perspective

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DRUG ADMIN., GUIDANCE FOR INDUSTRY: EVIDENCE-BASED REVIEW SYSTEM FOR SCIENTIFIC EVALUATION OF HEALTH CLAIMS (2009).

109. *See, e.g.*, sources cited *supra* notes 13–30.

beyond that obtained by separate analysis of each program.[110] This exercise is relevant to questions about the structure of food and medical product regulation, both in the United States and in other countries. It also implicates broader questions of institutional design, such as those addressed in the literature on the organization of government functions.[111] As David Hyman and William Kovacic have observed, analyzing the way policy tasks are assigned among agencies raises—in the public sector context—issues similar to those raised by Ronald Coase's *The Nature of the Firm*.[112] The appropriate boundaries of any individual government agency are not obvious, but they are issues of both academic interest and public importance.

For example, this Article emphasizes the striking similarities between the FDA-administered marketing authorization programs in highly disparate product categories. These similarities suggest that it matters where in a government a regulatory function is placed. Each of these programs might have developed differently if Congress had placed it in a different agency.

For clarity of analysis, this Article distinguishes between macro-level and micro-level organization of agency functions. It uses the term "macro-level organization of agency functions" to refer to the way policy functions are allocated among cabinet departments and agencies. It uses the term "micro-level organization of agency functions" to refer to the manner in which an individual agency structures its own activities. In other words, macro-level organization of agency functions refers to where policy functions fit on the entire federal government's organizational chart. Micro-level organization of agency functions refers to where policy functions assigned to an agency fit on that agency's organizational chart.

Over time, there have been significant changes in the location of regulatory functions that are today housed within the FDA. The Agency has been housed within the USDA, the Federal Security Administration, the Department of Health, Education, and Welfare (HEW), and today's

110. This is a complement to, not a substitute for, analysis of each individual program.

111. *See, e.g.*, David A. Hyman & William E. Kovacic, *Why Who Does What Matters: Governmental Design and Agency Performance*, 82 GEO. WASH. L. REV. 1446 (2014); David A. Hyman & William E. Kovacic, *Competition Agencies with Complex Policy Portfolios: Divide or Conquer?*, CONCURRENCES, no. 1-2013, at 9, 9–10 & n.6 [hereinafter Hyman & Kovacic, *Complex Policy Portfolios*] (listing prominent articles addressing issues of agency design by scholars in multiple academic fields).

112. *See* Hyman & Kovacic, *Complex Policy Portfolios*, *supra* note 111, at 10 (citing Ronald Coase, *The Nature of the Firm*, 4 ECONOMICA 286 (1937)) ("In a rough sense, we are taking a step toward sketching out the public administration equivalent of Ronald Coase's *Nature of the Firm*.").

Department of Health and Human Services.[113] The FDA has at times acquired functions from other agencies.[114] And Congress and the Executive have repeatedly made decisions about whether to assign specific regulatory functions to the FDA,[115] to assign them to other agencies, or to split the relevant authority between the FDA and other agencies.[116]

The FDA has been a model for many foreign regulatory agencies.[117] Its marketing authorization process for drugs has been especially influential.[118] However, even a quick look at other countries suggests that the macro-level organization used for these functions in the United States does not exhaust the possibilities for institutional design.

For example, some countries assign regulation of food and medical products to separate agencies, with numerous variations on this theme.[119] Proposals to do

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113. *Changes in Science, Law and Regulatory Authorities*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/about-fda/fda-history/changes-science-law-and-regulatory-authorities (Jan. 31, 2018) (describing the FDA's organizational history).

114. One significant example is the Department of Health, Education, and Welfare's (HEW's) decision to transfer biologics regulation from the National Institutes of Health (NIH) to the FDA. *See infra* notes 155–161 and accompanying text.

115. Examples include the decision to assign radiation control to the FDA in 1968, Radiation Control for Health and Safety Act of 1968, Pub. L. No. 90-602, 82 Stat. 1173 (1968), and tobacco control to the FDA in 2009, Family Smoking Prevention and Tobacco Control and Federal Retirement Reform, Pub. L. 111-31, 123 Stat. 1776 (2009).

116. Coordinated Framework for the Regulation of Biotechnology, 51 Fed. Reg. 23,302 (June 26, 1986) (dividing responsibility for regulation of agricultural biotechnology between the U.S. Department of Agriculture, the FDA, and the Environmental Protection Agency).

117. CARPENTER, *supra* note 22, at 686–726 (discussing the FDA's influence on foreign regulatory programs).

118. *Id.* at 696–722 (discussing the influence of the FDA's marketing authorization program for drugs in shaping drug regulation programs in other countries).

119. For example, the countries of the United Kingdom divide responsibility for medical products and food between separate agencies. The Medicines and Healthcare Products Regulatory Authority is responsible for many of the products that would be regulated as drugs, medical devices, and biologics in the United States. *See About Us*, U.K. MED. & HEALTHCARE PRODS. REGUL. AUTH., https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/about (last visited Aug. 16, 2022). For food, devolution of government functions has led to a set of devolved responsibilities split between two geographically focused agencies. *See generally Four-Country Working*, FOOD STANDARDS AGENCY (Dec. 22, 2020), https://www.food.gov.uk/about-us/four-country-working. The Food Standards Agency is responsible for food regulation in England, Wales, and Northern Ireland. *Id.* A separate public body, Food Standards Scotland, is responsible for food regulation in Scotland. *Id.* On the development of the U.K. Food Standards Agency, see John Krebs, *Establishing a Single, Independent Food Standards Agency: The United Kingdom's Experience*, 59 FOOD & DRUG L.J. 387 (2004).

something similar in the United States occur with some frequency, from multiple political perspectives, and with numerous different structures proposed.[120]

The framework presented in this Article suggests that there may be multiple factors that influence the FDA (and its congressional overseers) to mold its disparate marketing authorization functions into a smaller set of strikingly similar program types.[121] These may include basic efforts to treat like cases alike, the desire of both agency officials and congressional overseers

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At the supra-state level, the European Union divides its drug regulation and food regulation functions. It assigns drug regulation to the European Medicines Agency (EMA) and food regulation to the European Food Safety Authority (EFSA). The EMA is responsible for "authori[z]ing and monitoring medicines in the EU." *European Medicines Agency (EMA)*, EUROPEAN UNION, https://european-union.europa.eu/institutions-law-budget/institutions-and-bodies/institutions-and-bodies-profiles/ema_en (last visited Aug. 16, 2022). The EFSA "provides independent scientific advice on food-related risks." *European Food Safety Authority (EFSA)*, EUROPEAN UNION, https://european-union.europa.eu/institutions-law-budget/institutions-and-bodies/institutions-and-bodies-profiles/efsa_en (last visited Aug. 16, 2022). However, aspects of these functions, as well as other functions managed by the FDA in the United States, are regulated in the European Union at the member-state level. For example, most medical device regulation in the European Union is conducted at the member-state level, but the EMA does have a role in some aspects of the regulatory process. *See generally Medical Devices*, EUROPEAN UNION, https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices (last visited Aug. 16, 2022).

120. *See generally* Richard A. Merrill & Jeffery K. Francer, *Organizing Federal Food Safety Regulation*, 31 SETON HALL L. REV. 61, 115–18 (2000) (cataloging some of the more significant proposals from 1949 through 1998). For more recent discussions of this and related issues, see U.S. GOV'T ACCOUNTABILITY OFF., GAO-05-212, FOOD SAFETY: EXPERIENCES OF SEVEN COUNTRIES IN CONSOLIDATING THEIR FOOD SAFETY SYSTEMS (2005); U.S. GOV'T ACCOUNTABILITY OFF., GAO/T-RCED-99-256, FOOD SAFETY: U.S. NEEDS A SINGLE AGENCY TO ADMINISTER A UNIFIED, RISK-BASED INSPECTION SYSTEM (1999); Stuart M. Pape, Paul D. Rubin & Heili Kim, *Food Security Would Be Compromised by Combining the Food and Drug Administration and the U.S. Department of Agriculture into a Single Food Agency*, 59 FOOD & DRUG L.J. 405 (2004); Timothy M. Hammonds, *It Is Time to Designate a Single Food Safety Agency*, 59 FOOD & DRUG L.J. 427 (2004); and Note, *Reforming the Food Safety System: What if Consolidation Isn't Enough?*, 120 HARV. L. REV. 1345 (2007). While these publications focus on whether (and, if so, in what agency) food regulation should be consolidated, any such action would have implications for medical product regulation as well. This would come either from the FDA acquiring new responsibilities or losing its food-regulation function. As Merrill and Francer discuss in detail, *supra*, a decision to move food regulation out of the FDA would require numerous decisions as to which other programs (such as food additives, color additives, animal drugs, and dietary supplements) would be moved out of the FDA as well. In other words, while marketing authorization is not required for food itself, there are numerous food-related programs where marketing authorization is an important component.

121. *See infra* Part II.D (discussing numerous examples).

to rely on administrative structures with which they have experience, and phenomena such as path dependence and IPL.[122]

Overall, cross-category analysis suggests that the structure of marketing authorization programs is influenced by other programs administered by the same agency and overseen by the same congressional committees.[123] While this Article does not address agency functions beyond marketing authorization, it seems likely that other agency functions could be subject to similar influences.

This suggests that those considering changes to the macro-level organization of food and medical product regulation should be sensitive to the influence of other programs housed within the relevant agencies. Cross-category analysis does not itself point either in favor of, or against, the various proposals to change which regulatory functions are located within the FDA. It does, however, suggest that those proposing change should consider possible interaction, over time, between different programs administered by a single agency. It also suggests that moving a program from one agency to another may be the type of exogenous shock that could shift a program away from a seemingly path-dependent course.[124]

D. Interchangeable-Part Lawmaking

The framework's fourth contribution is to highlight a previously overlooked phenomenon, IPL. IPL occurs when a government takes a portion of its law in one subject area and uses it as a model for its own law in another subject area. It bears some similarity to what comparative lawyers describe as a "legal transplant," but it occurs wholly within a single government.

Comparative lawyers use the term "legal transplant" to describe situations where some part of a legal system in one country becomes a formal part of the legal system in another country.[125] This can be something as large as a legal tradition,[126] as small as an individual legal rule, or something between

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122. *See infra* Part II.D (discussing IPL).

123. On the influence of congressional committee structures on government programs, see generally Michael Doran, *Legislative Organization and Administrative Redundancy*, 91 B.U. L. REV. 1815 (2011).

124. On the relationship of path dependence theory to the issues addressed in this Article, see *infra* notes 188–195 and accompanying text.

125. The classic work on this topic is Alan Watson's 1974 book, *Legal Transplants*. *See* ALAN WATSON, LEGAL TRANSPLANTS: AN APPROACH TO COMPARATIVE LAW 21–30 (1974) [hereinafter WATSON 1974]; *see also* ALAN WATSON, LEGAL TRANSPLANTS: AN APPROACH TO COMPARATIVE LAW 21–30 (2d ed. 1993). For an assessment of the influence of Watson's book, see John W. Cairns, *Watson, Walton, and the History of Legal Transplants*, 41 GA. J. INT'L & COMP. L. 637 (2013).

126. *See, e.g.*, WATSON 1974, *supra* note 125, at 29–30 (discussing transplants of "an entire

those extremes.[127] It can be adopted willingly by the recipient country[128] or imposed by an outside power.[129] Willing adoption can take place through any method recognized by the recipient legal system. Methods recognized by many legal systems include legislative action, judicial decision, executive action, or constitutional revision. Comparative lawyers focus on legal transplants that occur between countries. There are, however, related phenomena that do not quite merit the transplant term.[130]

For example, in addition to the traditional legal transplant, there is the "transplantation" of law that takes place between sister states of a federal system. This can take place when one state adopts a sister state's approach to a particular area of law. This is a natural outcome of the idea that individual states serve as laboratories of democracy, free to choose their own approaches or follow the lead of another state. This can also take place when a new state is admitted to a federal union, and that state's constitution-drafters duplicate some aspects of the constitutional structures of existing sister states. As this does not carry as much risk of systemic rejection as country-to-country transplants, the "legal transplant" metaphor is not typically used. It is a phenomenon similar to the legal transplant referenced by comparative lawyers. However, it operates within a federal system.[131]

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legal system or a large portion of it"). On the idea of legal traditions, see generally MARY ANN GLENDON, PAOLO G. CAROZZA & COLIN B. PICKER, COMPARATIVE LEGAL TRADITIONS: TEXT, MATERIALS AND CASES ON WESTERN LAW 33–62 (4th ed. 2014), for a discussion on the concept of the legal tradition and the role of legal traditions in the study of comparative law. On the transplantation of entire legal traditions, see generally JOHN HENRY MERRYMAN & ROGELIO PÉREZ-PERDOMO, THE CIVIL LAW TRADITION: AN INTRODUCTION TO THE LEGAL SYSTEMS OF EUROPE AND LATIN AMERICA 4–5 (2019) for a description of the spread of the common law tradition by the British Empire and the civil law tradition by the Continental European empires.

127. For a recent review of academic work on legal transplants, see Toby S. Goldbach, *Why Legal Transplants?*, 15 ANN. REV. L. & SOC. SCI. 583 (2019).

128. Examples include the decision by many countries to adopt corporate laws modeled on the law of a U.S. state or another country. *See, e.g.*, Katharina Pistora, Yoram Keinan, Jan Kleinheisterkamp, & Mark D. West, *Evolution of Corporate Law and the Transplant Effect: Lessons from Six Countries*, 18 WORLD BANK RSCH. OBSERVER 89, 97–99 (2003) (discussing six countries that each took its corporate law as a transplant from a U.S. state or another country).

129. The most prominent example is the decision by the Allied Powers to impose a new Constitution on Japan following the end of the Second World War.

130. *Cf.* Nou & Nyarko, *supra* note 36 (drawing a similar analogy to the legal transplant literature in formulating their concept of "regulatory diffusion").

131. If one were searching for surgical metaphors, one could distinguish between "homologous" legal transplants between nation-states and "autologous" legal transplants within a federal system. But, while the analogy might be worth observing in a footnote, the payoff is likely insufficient to justify new terminology.

There is also another related phenomenon, more distant from the legal transplant, of interest to comparative lawyers. This occurs when a government takes a portion of its law in one subject area and uses it as a model for its own law in another subject area. This is an important phenomenon, but it is insufficiently disruptive to deserve the transplant metaphor. Instead, this is a more run-of-the-mill process that fits better with a metaphor suggesting manufacturing rather than surgery. This Article accordingly adopts the term IPL to describe situations where a government takes a portion of its law in one subject area and uses it as a model for its own law in another subject area.[132]

To put this concept in context, international legal transplants have been an important aspect of comparative law scholarship for decades. "Transplants" between sister states have been a foundational assumption of most federal systems and are involved in all situations where one sister state chooses to adopt an approach to a legal rule pioneered by another sister state. Most state-level law reform efforts and associated academic scholarship involve contemplated "transplants" between sister states. IPL, however, has up to this point been overlooked.

IPL has played a fundamental role in the FDA's regulatory structure.[133] This can be seen through an examination of the pathways and designations described earlier.[134] Congress has rarely cut from new cloth when expanding the FDA's marketing authorization role. It has, instead, drawn from existing marketing authorization programs, building new programs largely, but not entirely, out of preexisting models in other FDA-regulated fields. These are, in a sense, "autologous" regulatory transplants—they are transplants of existing agency programs into different portions of the same agency's regulatory portfolio. Congress has occasionally introduced new parts, but even these tend to be used simply to modify some part of an existing program that Congress does not wish to move into the new area. As set out further below, this can be seen from a brief review of congressional passage and agency implementation of marketing authorization requirements.

The concept of IPL may be particularly important in other situations where agencies have a role in statutory drafting. These situations may be surprisingly common. Recent empirical work has demonstrated that agencies have an

132. This can include both situations where IPL occurs within an individual agency (as discussed in this Part) and situations where IPL involves one agency taking an interchangeable part from a program or policy developed by another agency. It accordingly includes, but is not limited to, what Nou and Nyarko term "regulatory diffusion." *See* Nou & Nyarko, *supra* note 37.

133. This Article does not consider whether IPL can be found in other areas of U.S. federal regulation. This is an important topic for future work.

134. *See supra* Part I.A (pathways) and Part I.B (designations).

underappreciated role in drafting statutory text.[135] The concept of IPL is also relevant to recent political science work analyzing text reuse by legislatures.[136]

Congress first imposed an FDA-administered marketing authorization requirement, for drug safety, in the FFDCA.[137] It imposed this requirement by defining the term "new drug" in FFDCA § 201(p)[138] and imposing this safety-review requirement on all drugs that were "new" within the meaning of the § 201(p) definition. When, in 1962, Congress decided that the FDA should review drugs for efficacy as well as safety, it did this largely by changing "safe" to "safe and effective" in the new drug definition.[139]

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135. *See, e.g.*, Jarrod Shobe, *Agencies as Legislators: An Empirical Study of the Role of Agencies in the Legislative Process*, 85 GEO. WASH. L. REV. 451, 472–76 (2017); Christopher J. Walker, *Legislating in the Shadows*, 165 U. PA. L. REV. 1377, 1387–96 (2017); Ganesh Sitaraman, *The Origins of Legislation*, 91 NOTRE DAME L. REV. 79, 104–05 (2015).

These articles followed a groundbreaking, two-part empirical study of the role of congressional staff in drafting both text and legislative history. *See* Abbe R. Gluck & Lisa Schultz Bressman, *Statutory Interpretation from the Inside—An Empirical Study of Congressional Drafting, Delegation, and the Canons* (pts. 1 & 2), 65 STAN. L. REV. 901 (2013), 66 STAN. L. REV. 725 (2014). Related follow-on work has analyzed the statutory interpretation process within agencies (as opposed to courts, which have been the traditional subject of academic work on statutory interpretation). *See, e.g.*, Christopher J. Walker, *Inside Agency Statutory Interpretation*, 67 STAN. L. REV. 999 (2015) (reporting the results of an empirical survey of the way agency officials approach statutory interpretation during the rulemaking process); *cf.* Jennifer Nou, *Intra-Agency Coordination*, 129 HARV. L. REV. 421 (2015).

With respect to FDA specifically, Hutt et al., *supra* note 15, at 610, observe that a 1967 proposal for granting the FDA a marketing authorization role for medical devices was "drafted by the FDA's legislative office, which had consulted with many interest groups." *Id.* This suggests that the FDA has been involved in statutory drafting for at least half a century.

136. *See, e.g.*, Roy Gava, Julien M. Jaquet & Pascal Sciarini, *Legislating or Rubber-Stamping? Assessing Parliament's Influence on Law-Making with Text Reuse*, 60 EUR. J. POL. RES. 175 (2021); Frindolin Linder, Bruce Desmarais, Matthew Burgess & Eugenia Giraudy, *Text as Policy: Measuring Policy Similarity Through Bill Text Reuse*, 48 POL'Y STUD. J. 546 (2018); John Wilkerson, David Smith & Nicholas Stramp, *Tracing the Flow of Policy Ideas in Legislatures: A Text Reuse Approach*, 59 AM. J. POL. SCI. 943 (2015). These political science methodologies have, to this point, had only limited impact in the law journal literature. A February 22, 2022, search of the Westlaw "Law Reviews and Journals" database with the search string "text /2 (reuse re-use 're use')" returned only 21 results.

137. While Congress had imposed a marketing authorization requirement for biologics in 1902, *see* Biologics Control Act of 1902, Pub. L. No. 57-244, 32 Stat. 728 (1902), the FDA did not yet exist at that time. On the transfer of biologics regulation from NIH to the FDA in the 1970s, see *infra* notes 156–162and accompanying text.

138. FFDCA § 201(p), 21 U.S.C. § 321(p).

139. Drug Amendments of 1962 (Kefauver-Harris Amendments), Pub. L. No. 87-781, sec. 102(a)(1), § 201(p)(1), 76 Stat. 780, 781 ("Section 201(p)(1) of the [FFDCA] . . . defining

The 1938 version of FFDCA § 201(p) defined as "new"—and thus subject to the FDA's first marketing authorization requirement—all drugs that were not "generally recognized as safe" (GRAS).[140] This is the original source of the GRAS requirement that is today central to food additives regulation.[141] With the 1962 adoption of an efficacy requirement for drugs, the GRAS concept was no longer sufficient to exempt drugs from marketing authorization. To avoid qualifying as new—and thus triggering the marketing authorization requirement—drugs would henceforth need to be "generally recognized as both safe and effective" (GRASE).[142] This is the origin of the GRASE requirement.

This GRASE requirement was one of two statutory concepts that drove the FDA's multi-decade effort to implement the efficacy requirement for drugs. The other was a statutory requirement that such efficacy be shown by "substantial evidence" and defining substantial evidence to mean "evidence consisting of adequate and well-controlled investigations."[143] The

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the term 'new drug', is amended by (A) inserting therein, immediately after the words 'to evaluate the safety', the words 'and effectiveness', and (B) inserting therein, immediately after the words 'as safe', the words 'and effective.'").

140. FFDCA, Pub. L. No. 75-717, 52 Stat. 1040, 1041–42 (1938) ("The term 'new drug' means—(1) Any drug the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe for use under the conditions prescribed, recommended, or suggested in the labeling thereof . . . ."). A grandfathering provision exempted certain drugs from this "new drug" definition. *Id.* at 1042. The exempted drugs were those lawfully marketed under the Food and Drugs Act, Pub. L. No. 59-384, 34 Stat. 768 (1906), so long as they remained unchanged since the passage of the FFDCA, Pub. L. No. 75-717, 52 Stat. 1040 (1938).

141. *See* Food Additives Amendment of 1958, Pub. L. No. 85-929, sec. 2, § 201(s), 72 Stat. 1784, 1784 (1958) (promulgating new definition of "food additive" that exempted substances "generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use" from regulation as food additives).

142. *See* Kefauver-Harris Amendments, Pub. L. No. 87-781, sec. 102(a)(1), § 201(p)(1), 76 Stat. 780, 780–81.

143. *Id.* sec. 102(a)(1), § 505(d), 76 Stat. at 781 (requiring denial of a new drug application if the FDA finds that "evaluated on the basis of the information submitted to [the FDA] as part of the application and any other information before [the FDA] with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof"); *id.* ("As used in this subsection and subsection (e), the term 'substantial evidence' means evidence consisting of adequate and well-controlled

GRASE concept was the organizing principle for applying the efficacy requirement to drugs already on the market at the time the Kefauver-Harris Amendments became law.[144] The FDA's initial focus was on applying the GRASE concept to prescription drugs.[145] Later, the FDA began a similar process of applying the GRASE concept to over-the-counter (OTC) drugs.[146] This resulted in the development of the OTC monograph system, a process which governed OTC drugs from the 1970s through today.[147]

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investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."). As part of this implementation, the FDA promulgated a famously rigorous interpretation of "adequate and well-controlled clinical investigations." Hearing Regulations and Regulations Describing Scientific Content of Adequate and Well-Controlled Clinical Investigations, 35 Fed. Reg. 7250 (May 8, 1970). The current text of the requirement for adequate and well-controlled investigations for drugs is found at 21 C.F.R. § 314.126. For consolidated excerpts of most of the documents referenced in this footnote, see MUCHMORE, *supra* note 2, at 319–24.

144. The FDA did this by subcontracting the first stage of the process to the National Research Council of the National Academy of Sciences (NAS-NRC). The NAS-NRC was tasked with making initial determinations as to how likely it was that a drug was generally recognized as both safe and effective (GRASE). The FDA then used the NAS-NRC evaluations to determine which drugs it should propose to withdraw from the market unless those seeking to continue to market the drug came forward with evidence meeting the substantial evidence of efficacy standard. *See* Reports of Information for Drug Effectiveness, 31 Fed. Reg. 9426 (July 9, 1966) (announcing NAS-NRC role in implementation of drug efficacy requirement). The U.S. Supreme Court approved this process in a series of four decisions—all handed down on the same day—that came to be known as the 1973 quartet. *See* MUCHMORE, *supra* note 2, at 324–25. The four cases of the quartet were Weinberger v. Hynson, Westcott & Dunning, Inc., 412 U.S. 609 (1973); CIBA Corp. v. Weinberger, 412 U.S. 640 (1973); Weinberger v. Bentex Pharm. Inc., 412 U.S. 645 (1973); and USV Pharm. Corp. v. Weinberger, 412 U.S. 655 (1973).

145. *See* Proposal Establishing Rule Making Procedures for Classification, 37 Fed. Reg. 85 (proposed Jan. 5, 1972).

146. *See id.*; Procedures for Classifying Over-the-Counter Drugs, 37 Fed. Reg. 9464 (May 11, 1972).

147. The OTC monograph system is set to change significantly over the coming years, as Congress included a major statutory revision in the March 2020 COVID-19 economic stimulus bill. *See* Coronavirus Aid, Relief, and Economic Security (CARES) Act, Pub. L. No. 116-36, sec. 3851, § 505G, sec. 3852, § 502, sec. 3853, § 586C, H, sec. 3855, 134 Stat. 281, 435–58 (2020). The CARES Act codifies the new statutory structure for OTC drugs primarily at FFDCA § 505G, 21 U.S.C. § 355h. For an overview, see ELAYNE J. HEISLER, EVELYN P. BAUMRUCKER, CLIFF BINDER, KRISTEN J. COLELLO, AGATA DABROWSKA, PATRICIA A. DAVIS ET AL., CONG. RSCH. SERV., R46334, SELECTED HEALTH PROVISIONS IN TITLE III OF THE CARES ACT (P.L. 116-136), at 55–59 (2020).

When Congress chose in 1958 to require marketing authorization for food additives—and to do so in a manner that left many existing additives on the market—it adopted the GRAS concept it had introduced in the 1938 FFDCA "drug" definition.[148] Congress then took the original Delaney Clause, introduced with the regulation of food additives, and incorporated similar provisions in the regulatory regimes it developed for color additives in 1960[149] and animal drugs in 1968.[150]

In 1968, a broader reform accompanied Congress's adoption of the just-mentioned animal drugs Delaney Clause. In the Animal Drug Amendments, Congress carved out "animal drugs" as a separate product category.[151] The drug definition, within the FFDCA, explicitly includes both human and animal drugs.[152] To subject some animal-specific drugs to a separate marketing authorization regime—without removing animal drugs from the "drug" definition—Congress adopted a technique from the drug-regulation tool bin. It

148. *Compare* FFDCA, Pub. L. No. 75-717, 52 Stat. 1040, 1041–42 (1938) ("The term 'new drug' means—(1) Any drug the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe for use under the conditions prescribed, recommended, or suggested in the labeling thereof . . . ."), *with* Food Additives Amendment of 1958, Pub. L. 85-929, sec. 2 § 201(s), 72 Stat. 1784, 1784 ("The term 'food additive' means any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food . . . , if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures . . . to be safe under the conditions of its intended use"). This basic structure remains in place today, with the modification that the "new drug" definition of FFDCA § 201(p), 21 U.S.C. § 321(p), has, since 1962, relied on the GRASE concept rather than the "generally recognized as safe" (GRAS) concept. *Compare* FFDCA § 201(p), 21 U.S.C. § 321(p) (excluding GRASE substances from the definition of "new drug"), *with* FFDCA § 201(s), 21 U.S.C. § 321(s) (excluding GRAS substances from the definition of "food additive").

149. *See* Color Additive Amendments of 1960, Pub. L. No. 86-618, sec. 103, § 706(b)(5)(A),74 Stat. 397, 400 (promulgating a new statutory regime for color additives).

150. *See* Animal Drug Amendments Act of 1968, Pub. L. No. 90-399, sec. 101(a), § 512(a)(1)(H), 82 Stat. 342, 345 (promulgating a new statutory regime for animal drugs).

151. *See id.* This statute did not modify the drug definition in FFDCA § 201(g), 21 U.S.C. § 321(g). Instead, it created a separate definition of "new animal drug" to be codified at FFDCA § 201(w), 21 U.S.C. § 321(w). *See* Animal Drug Amendments of 1968, sec. 102, § 201(w)–(x), 82 Stat. at 351–52. On the development of animal drugs as a separate product category, see Lambert, *supra* note 16, at 277–78.

152. *See* FFDCA § 201(g)(1), 21 U.S.C. § 321(g)(1). This is sensible, as some human drugs are also used for animals.

created a separate definition of "new animal drug"[153] and excluded items qualifying as "new animal drug[s]" from the earlier "drug" definition.[154] In setting the marketing authorization standard for animal drugs, Congress adopted another technique from the drug-regulation tool bin. It turned again to the statutory concepts of "substantial evidence" of efficacy through "adequate and well-controlled investigations."[155]

A more dramatic example of IPL took place in 1972. This involved a decision by the HEW[156] to move its biologics regulation function from the National Institutes of Health (NIH) to the FDA. At the time, biologics regulation had been a function of the NIH and its predecessors for seventy years—first under the Biologics Control Act of 1902,[157] then under the Public Health Services Act.[158] In the early 1970s, congressional and General Accounting Office (GAO)[159] investigations exposed significant problems with the biologics regulation program then administered by NIH's Division of Biologics Standards (DBS).[160] Following these revelations, HEW transferred DBS to the FDA, where it began its new life as the FDA's new Bureau of Biologics.[161] The FDA then

153. *See* Animal Drug Amendments Act of 1968, 82 Stat. at 351–52 (codified at FFDCA § 201(v), 21 U.S.C. § 321(v)).

154. *See* FFDCA § 201(g)(1), 21 U.S.C. § 321(g)(1).

155. *See, e.g.*, Animal Drug Amendments Act of 1968, 82 Stat. at 345 (codified at FFDCA § 512, 21 U.S.C. § 360b). The structure of FFDCA § 512, 21 U.S.C. § 360b, on new animal drugs, is strikingly similar to FFDCA § 505, 21 U.S.C. § 355, on new drugs. However, a more detailed reading reveals substantial differences. In particular, the new animal drugs provision does not require human clinical trials (for obvious reasons) and focuses less on the safety of the drug for its recipient (an animal) than on the safety of a human who might later consume the animal or its byproducts.

156. At the time, both the FDA and NIH were housed within HEW. HEW became today's Department of Health and Human Services when Congress chose to carve off its education functions as a separate, cabinet-level Department of Education.

157. *See* Biologics Control Act of 1902, Pub. L. No. 57-244, 32 Stat. 728 (1902).

158. *See* Public Health Service Act, Pub. L. No. 78-410, 58 Stat. 682 (1944).

159. The General Accounting Office (GAO) was the predecessor to today's Government Accountability Office. *100 Years of GAO*, U.S. GOV'T ACCOUNTABILITY OFF., https://www.gao.gov/about/what-gao-does/hundred-years-of-gao (last visited Aug. 16, 2022). The name change took place in 2004. *Id.*

160. *See* Nicholas Wade, *DBS: Agency Contravenes its Own Regulation*, SCIENCE 34, 34–35 (1972) (describing congressional and GAO investigations of DBS vaccine regulation); *see also* Nicholas Wade, *Division of Biologics Standards: Reaping the Whirlwind*, SCIENCE 162, 162–64 (1973) (describing additional DBS problems and some of the litigation that followed). For a recent discussion of some of the key events and figures involved, see MEREDITH WADMAN, THE VACCINE RACE 246, 246–52 (2017).

161. *See* Statement of Organization, Functions, and Delegations of Authority, 37 Fed. Reg. 12,865 (June 29, 1972).

began a long process of digesting this new regulatory role.[162]

By contrast, when Congress imposed a marketing authorization process for medical devices in 1976, it chose to rely only lightly on IPL. The obvious area from which to obtain an interchangeable part was drug regulation, where a marketing authorization regime—requiring a showing of both safety and efficacy—had been developing since 1962. However, Congress deliberately chose not to rely heavily on the "drug model."[163] Instead, Congress used a more permissive marketing authorization standard.[164] It also sought to constrain agency discretion with a highly detailed statute,[165] to

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162. The FDA first took steps to apply the "drug" provisions of the FFDCA, FFDCA § 201(g)(1), 21 U.S.C. § 321(g)(1) (1970), to biologics. Procedures for Review of Safety, Effectiveness, and Labeling, 37 Fed. Reg. 16,679 (proposed Aug. 18, 1972). The agency did this by determining that "all biological products are drugs" under the FFDCA. *Id.* At the same time, it began a long process of determining how to apply the statutory efficacy requirement to biologics, and how that FFDCA requirement would interact with the safety, purity, and potency applicable to biologics under PHSA § 351, 42 U.S.C. § 262. Its later actions included merging its Bureau of Biologics into its Bureau of Drugs, *see* Statement of Organization, Functions, and Delegations of Authority, 47 Fed. Reg. 26,913 (June 22, 1982), and then separating them into today's Center for Biologics Evaluation and Research (CBER) and Center for Drug Evaluation and Research (CDER). Statement of Organization, Functions, and Delegations of Authority, 52 Fed. Reg. 38,275 (Oct. 15, 1987). These actions also included merging separate biologics Product License Applications and Establishment License Applications into a single Biologics License Application, *see* Biological Products Regulated Under Section 351 of the Public Health Service Act; Implementation of Biologics License; Elimination of Establishment License and Product License, 64 Fed. Reg. 56,441 (Oct. 20, 1999), and transferring regulatory responsibility for various biological products between CBER and CDER. *See, e.g.*, Drug and Biological Product Consolidation, 68 Fed. Reg. 38,067 (proposed June 26, 2003). For consolidated excerpts of most of the documents referenced above, see MUCHMORE, *supra* note 2, at 459–66.

163. *See* Merrill, *supra* note 26, at 1806 (quotation marks in original omitted); *id.* 1806–08 (describing some of the background that led to Congress's decision not to model the device-regime directly on the drug-regulation regime).

164. *Compare* FFDCA § 505(d), 21 U.S.C. § 355(d), *with* FFDCA § 515(c), 21 U.S.C. § 360e(c). In addition to this more permissive standard, Congress permitted the FDA to rely on a broader range of evidence than that permitted for New Drug Applications. *See* Merrill, *supra* note 26, at 1821–23 (noting that Congress used language in the premarket approval provisions of the Medical Device Amendments permitting the FDA to rely on "evidence that has not been derived from controlled clinical studies of the sort [Congress] has prescribed for new drugs").

165. *See* Merrill, *supra* note 26, at 1808 (noting that the Medical Device Amendments "reflected an effort to anticipate and resolve most questions about FDA's authority and about the obligations of device makers"). This effort was spectacularly unsuccessful. The FDA interpreted the statute aggressively, and Congress eventually revised the statute to align more

structure the regulatory program around device types rather than individual devices,[166] and to develop a system of premarket approval that it hoped would avoid a set of then-perceived problems with the drug model.[167]

Congress's new approach for medical devices experienced some growing pains. It seems fairly clear that Congress envisioned a system where, after an initial period of implementation, most medical devices would be authorized for marketing through the paradigm pathway, premarket approval. However, the FDA did not take this approach in implementing the Medical Device Amendments of 1976.[168] Instead, the FDA based its marketing authorization program around an alternate pathway, the substantial equivalence process, that the FDA developed through a fairly aggressive reading of two statutory provisions.[169]

The FDA's decision led to tension between Congress, the GAO, and the FDA throughout much of the 1980s.[170] There were multiple critical GAO reports and congressional hearings,[171] but it became apparent to most involved that the FDA had insufficient resources to implement a marketing authorization program for devices that matched the statutory scheme. In 1990, Congress effectively caved and accepted the FDA's preferred approach.[172] The Safe Medical Devices Act of 1990 modified the relevant FFDCA provisions to align better with the marketing authorization program the FDA had developed.[173]

Yet, despite these growing pains with medical device regulation, Congress worked primarily from the medical devices toolkit when it granted the FDA authority over tobacco products.[174] Like with medical devices, the FDA's

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closely with the FDA's approach to medical device regulations. *See* DEGNAN, *supra* note 15, at 121–26; Safe Medical Devices Act of 1990, Pub. L. No. 101-629, 104 Stat. 4511.

166. *See* Merrill, *supra* note 26, at 1808–10.

167. *See id.* at 1800, 1811–12 (describing the FDA's effort to implement the Medical Device Amendments in a manner that would not mirror the marketing authorization regime applicable to drugs).

168. The story has been told many times. For a concise version, see generally DEGNAN, *supra* note 15, at 114–28.

169. *See id.* at 121–24. The first was FFDCA § 510(k), 21 U.S.C. § 360. This provision required medical device establishments to register annually with the FDA, and—almost incidentally—required those registered to notify the FDA before marketing a new device. The second was FFDCA § 510(f)(1), 21 U.S.C. § 360(f)(1), which classified those devices that were not substantially equivalent to preamendments devices into Class III. *Id.*

170. *See* DEGNAN, *supra* note 15, at 124–26.

171. *See id.*

172. *See id.* at 126.

173. *See id.* (describing, among other changes, the addition of § 513(i) to the FFDCA).

174. *See* Family Smoking Prevention and Tobacco Control Act (TCA), Pub. L. No. 111-31, 123 Stat. 1776 (2009).

authority over tobacco products uses a paradigm pathway based on premarket approval and an alternate pathway based on substantial equivalence.[175] However, the trigger for regulation uses a technique that combines device-regulation and drug-regulation tools. It is structured as a newness provision, which at first sounds similar to the statutory definition of "new drug."[176] However, the provision itself is a date-based grandfathering provision similar to the one Congress used for medical devices.[177]

Another major area where Congress has relied on IPL is in its implementation of user fees to fund the FDA's marketing authorization programs. Congress first enacted a user fee program for prescription drugs in 1992.[178] It enacted similar programs for medical devices in 2002,[179] animal drugs in 2008,[180] generic drugs in 2012,[181] biosimilar and interchangeable biological products in 2012,[182] and OTC drugs in 2020.[183] The user fee programs appear unlikely to disappear. While each has a sunset provision, Congress has chosen to renew the programs each time they have come up for reauthorization. They now fund a substantial portion of the FDA's product-review staff; renewals are typically described as "must pass" legislation.[184]

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175. *See* MUCHMORE, *supra* note 2, at 102–03, 111–12.

176. FFDCA § 201(p), 21 U.S.C. § 321(p).

177. *Compare* FFDCA § 910(a)(1), 21 U.S.C. § 387j(a)(1) (defining new tobacco products to include "any tobacco product (including those products in test markets) that was not commercially marketed in the United States as of February 15, 2007"), *with* FFDCA § 513(f)(1)(A), 21 U.S.C. § 360c(f)(1)(A), *and* FFDCA § 515(b)(1)(A), 21 U.S.C. § 360e(b)(1)(A) (basing certain marketing authorization requirements on whether a device was in commercial distribution "before May 28, 1976"). On the FDA's decision to interpret the "as of" language in the TCA as referring only to products marketed on that specific date, see U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: ESTABLISHING THAT A TOBACCO PRODUCT WAS COMMERCIALLY MARKETED IN THE UNITED STATES AS OF FEBRUARY 15, 2007, at 3 (2014).

178. Prescription Drug User Fee Act of 1992, Pub. L. No. 102-571, sec. 103, §§ 735, 736, 106 Stat. 4491.

179. Medical Device User Fee and Modernization Act of 2002, Pub. L. No. 107-250, sec. 102, §§ 737, 738, 116 Stat. 1588.

180. Animal Drug User Fee Amendments of 2008, sec. 103, §740(a), Pub. L. No. 110-316, sec. 102, § 739, sec. 103, § 740(a), (b)(1)–(3), (c), (g)(3)(A)–(E), (g)(4), sec. 104, § 740(A), 122 Stat. 3509; Animal Generic Drug User Fee Act, Pub. L. No. 110-316, sec. 202, §§ 741, 742, 122 Stat. 3509, 3515 (2008).

181. Generic Drug User Fee Amendments of 2012, Pub. L. No. 112-144, sec. 302, §§ 744A, 744B, sec. 303, § 744C, sec. 306, § 502, sec. 307, § 714, sec. 308, § 715, 126 Stat. 1008.

182. Biosimilar User Fee Act of 2012, Pub. L. No. 112-144, § 401, sec. 402, §§ 744G, 744H, sec. 403, § 744I, sec. 407, § 735, sec. 408, § 715, 126 Stat. 993, 1026.

183. CARES Act, Pub. L. No. 116-136, sec. 3851, § 505G, 134 Stat. 281, 435–54 (2020).

184. AGATA BODIE & AMANDA K. SARATA, CONG. RSCH. SERV., R44750, FDA HUMAN MEDICAL PRODUCT USER FEE PROGRAMS: IN BRIEF 2 (2017).

The foregoing discussion has demonstrated the degree to which many of the FDA's regulatory programs are deliberately built from component parts taken from existing programs. This interchangeable-part structure suggests two things. First, analysis limited to a single product category will obscure relationships that are more apparent through the framework developed in this Article. Second, it is not infrequent for regulatory techniques developed for one product category to be selected by Congress for insertion elsewhere in the regulatory scheme. This suggests that existing programs—even small ones—should not be viewed solely as aspects of their narrow regulatory field. Each one also serves as a potential model for revision of existing programs or creation of new ones.

Why does such an interchangeable-part structure develop? A full explanation is beyond the scope of this Article. One likely factor, however, is tied to the FDA participating in the lawmaking process.[185] Put simply, FDA officials comfortable with administering specific statutory language are likely to consider recommending similar language to Congress for future regulatory programs.

As the empirical work discussed above has demonstrated, the FDA is far from the only agency in regular dialogue with Congress about possible revisions to statutory text. Officials at other agencies likely have similar incentives to use text they are comfortable administering as a basis for proposed statutory revisions. Accordingly, IPL likely plays a role in many statutes administered by other agencies as well.

The likely presence of IPL in other substantive fields suggests a number of directions for future research. One, open to those with detailed knowledge of specific agency-administered statutes, is a project similar to the one undertaken in this section. Close reading of statutes administered by other agencies may reveal similar patterns of IPL. If this is the case, it could establish that IPL plays a major—and previously unappreciated—role in the creation of statutory text.

A second research direction is open to those comfortable working with large datasets and computer-assisted language-processing techniques. This approach could search for IPL across federal law more broadly.[186] It could potentially reveal IPL both within individual agencies and between different agencies.[187]

Finally, there may be a relationship between IPL and path dependence theory. In recent decades, legal scholars have used the concept of path dependence as a partial explanation for the structure of

185. On agency participation in statutory drafting, see *supra* note 135.

186. *Cf.* Nou & Nyarko, *supra* note 36 (analyzing the related concept of "regulatory diffusion" in rulemaking by U.S. federal agencies over a 20-year period).

187. This type of work could, for example, employ some of the techniques that have been used by political scientists analyzing text-reuse by legislators. *See supra* note 136.

existing institutions.[188] This effort builds on the work of scholars in related fields, especially those working in economics[189] and political science.[190] Much of this work has focused on the role of path dependence in a common law system, but some work has also touched on the role of statutes in path dependence.

IPL may be an important component of the way that path dependence operates in the FDA's regulatory programs.[191] First, common experience suggests that the structure of existing regulatory programs provides the starting point for most discussions of possible reform. Second, the phenomenon of increasing returns provides an incentive to re-use existing regulatory techniques where possible, rather than create new ones.[192] This is, in effect, an economy of scope—a cost savings that results from an increase in the scope, rather than the scale, of a particular undertaking.[193] In many situations, repurposing an existing regulatory technique is likely to be less expensive than developing a new regulatory technique from scratch.[194]

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188. *See, e.g.*, Oona Hathaway, *Path Dependence in the Law: The Course and Pattern of Legal Change in a Common Law System*, 86 IOWA L. REV. 601 (2001); Mark Roe, *Chaos and Evolution in Law and Economics*, 109 HARV. L. REV. 641 (1996); Clayton P. Gillette, *Lock-in-Effects in Law and Norms*, 78 B.U. L. REV. 813 (1998).

189. *See, e.g.*, PIERSON, *supra* note 86; W. BRIAN ARTHUR, INCREASING RETURNS AND PATH DEPENDENCE IN THE ECONOMY (1994); DOUGLASS C. NORTH, INSTITUTIONS, INSTITUTIONAL CHANGE AND ECONOMIC PERFORMANCE (1990). For economists, a core concern is whether path dependence leads to lock-in of inefficient institutions. *See generally* S. J. Liebowitz & Stephen E. Margolis, *Path Dependence, Lock-In, and History*, 11 J.L. ECON. & ORG. 205 (1995) (suggesting that path dependence leads to inefficient institutions less frequently than has often been suggested). *Compare* Paul A. David, *Clio and the Economics of QWERTY*, 75 AM. ECON. REV. 332 (1985) (the classic article on path dependence leading to lock-in of inefficient institutions), *with* S. J. Liebowitz & Stephen E. Margolis, *The Fable of the Keys*, 33 J.L. & ECON. 1 (1990) (questioning empirical basis of claims in Paul David's 1985 article).

190. *See, e.g.*, Paul Pierson, *Increasing Returns, Path Dependence, and the Study of Politics*, 94 AM. POL. SCI. REV. 251 (2000) (suggesting that, in analysis of political institutions, path dependence provides value even in the absence of any claims of inefficient institutions because it provides an explanatory perspective that purely functional explanations cannot).

191. *Cf.* Katerina Linos & Melissa Carlson, *Qualitative Methods for Law Review Writing*, 84 U. CHI. L. REV. 213 (2017) (suggesting a need for more detailed analysis of the methods by which path dependence operates). If IPL is observed in other jurisdictions or regulatory fields, it could play a similar role in those areas as well.

192. This incentive should apply to both legislatures (in their lawmaking and oversight roles) and regulators.

193. *See* John C. Panzar & Robert D. Willig, *Economies of Scope*, 71 AM. ECON. REV. 268 (1981) (describing economies of scope and distinguishing them from economies of scale).

194. A detailed analysis of the role of path dependence and economies of scope is beyond

CONCLUSION

This Article has set out a framework for analysis of the FDA's marketing authorization programs. At the first level, the framework divides the FDA's marketing authorization programs into three components: pathways, designations, and means of access before marketing authorization. At the second level, the framework distinguishes between two types of pathways (paradigm and alternate), three types of designations (review clock, application assistance, and market exclusivity), and four means of access before marketing authorization (standard investigational use, expanded access, emergency use, and right-to-try access).

This framework makes four primary contributions. First, it provides a functional terminology for analysis of the FDA's marketing authorization programs. Second, it suggests that the "paradigms and alternatives" structure that can be seen at the FDA has developed, in part, to manage the tradeoff between Type I and Type II error in the FDA's marketing authorization decisions. Third, it suggests that there are substantive consequences to assigning particular government functions to one agency rather than another. Fourth, it highlights the role of a newly identified phenomenon, IPL, in the FDA's marketing authorization programs.

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the scope of this Article. The claim here is simply that IPL may play a role in the way path dependence operates. Accordingly, the relationship between IPL, path dependence, and economies of scope may be a fruitful area for future research.

APPENDICES

Appendix A: Pathways Chart

FIGURE 3:

PATHWAYS[195]		
Product Category	**Paradigm**	**Alternate**
Drug (not including biologic drugs)	- NDA under FFDCA § 505(b)(1)	- 505(b)(2) application - ANDA under FFDCA § 505(j) - accelerated approval under FFDCA § 506(c) - animal rule under 21 CFR § 314.610 - LPAD under FFDCA § 506(c)(1)(A) - certification process for "designated medical gases" under FFDCA § 576 - request for inclusion in OTC monograph under FFDCA § 505H(b)
Device	- PMA under FFDCA § 515(c)	- PMN under FFDCA § 510(k) - reclassification, under FFDCA § 513(e) or FFDCA § 513(f), to exempt from PMN - *de novo* classification, under FFDCA § 513(f)(2), to exempt from PMN - HDE under FFDCA § 520(m)

195. Statutory references in this Figure—as well as the other figures in this Article—are to the section numbers of the Federal Food, Drug, and Cosmetics Act of 1938, Pub. L. No. 75-717, 52 Stat. 1040 (1938), as amended, and the Public Health Services Act, Pub. L. No. 78-410, 58 Stat. 682 (1944), as amended. For a detailed chart providing, for each provision of the FFDCA, cross references to the corresponding U.S. code provisions, the date each provision was passed, and the date each was last amended, see ADAM I. MUCHMORE, FOOD AND DRUG REGULATION: STATUTORY AND REGULATORY SUPPLEMENT 27–56 (2021 ed.).

Food additive	- FFDCA § 409 food additives petition	- GRAS process resulting in exemption from definition under FFDCA § 201(s) - FFDCA § 409(h) notification for certain food-contact substances - exemption for food contact substance as below threshold of regulation under 21 C.F.R. § 170.39
Color additive	- color additive petition under FFDCA § 721(b)	N/A
Animal drug	- NADA under FFDCA § 512(b)(1)	- ANADA under FFDCA § 512(b)(2) - conditional approval under FFDCA § 571 - indexing under FFDCA § 572
Tobacco product	- premarket tobacco product application under FFDCA § 910(c)(2)	- substantial equivalence pathway under FFDCA § 910(a) - request for exemption from substantial equivalence requirement
Biological product	- biologics license application under PHSA § 351(a)(2)(C)	- biosimilar or interchangeable application under PHSA § 351(k)
Combination product	- pathways based on primary mode of action, with consultation with other relevant FDA offices	- pathways based on primary mode of action, with consultation with other relevant FDA offices

Appendix B: Designations Chart

FIGURE 4:

DESIGNATIONS			
Designation Type	**Designation Name**	**Potentially-Eligible Product Categories**	**Benefits**
Review clock	**Priority review**	Drugs (including biologic drugs)	- the FDA has *goal* of taking action on complete application within 6 months (rather than the 10-month goal the FDA has for standard review)
Application assistance	**Fast track**	Drugs (including biologic drugs)	- extra interaction with the FDA during review process (extra meetings, etc.) - potential eligibility for priority review - potential eligibility for rolling review
Application assistance	**Breakthrough therapy**	Drugs (including biologic drugs)	- concerted FDA effort to expedite development of drug through enhanced interaction, detailed advice, and early involvement by senior officials - potential eligibility for priority review - potential eligibility for rolling review

Application assistance	**Breakthrough device**	Devices	- extra interaction with the FDA, including review team support and early involvement of senior management - potential to balance pre-market data with post-market data - potential to streamline clinical trials in various ways - expedited review of manufacturing-process compliance issues - all breakthrough devices qualify for priority review
Application assistance	**Regenerative medicine advanced therapy (RMAT)**	Biologics and combination products that include a biologic component,	- all breakthrough therapy features - potential support for use of accelerated approval pathway - if accelerated approval granted, potential ability to satisfy post-approval requirements through evidence other than traditional clinical trials
Application assistance	**Priority zoonotic animal drug**	Animal drugs	- taking steps to make clinical trials more efficient, including steps that may reduce the number of animals needed for trials - extra interaction with the FDA, including review team support and early involvement of senior officials - involving senior officials in facilitating in cross-disciplinary review

Market exclusivity	**Orphan drug**	Drugs (including biological drugs)	7-year market exclusivity
Market exclusivity	**Qualified infectious disease product (QIDP)**	Drugs (not including biologic drugs)	5-years added to certain other market exclusivity periods
Market exclusivity	**Competitive generic therapy (CGT)**	Drugs (not including biologic drugs)	180 days market exclusivity
Market exclusivity	**Designated new animal drug for minor use or minor species**	Animal drugs	7 years market exclusivity

Appendix C: Means of Access Before Marketing Authorization Chart

Figure 5:

MEANS OF ACCESS BEFORE MARKETING AUTHORIZATION				
PRODUCT CATEGORY*	MEANS OF ACCESS			
	Standard Investigational Use	**Expanded Access**	**Emergency Use**	**Right to Try Access**
Drug	FFDCA § 505(i)	FFDCA § 561	FFDCA § 564	FFDCA § 561B
Device	FFDCA § 520(g)	FFDCA § 561	FFDCA § 564	N/A
Food additive	FFDCA § 409(j)	N/A	N/A	N/A
Color additive	FFDCA § 720(f)	N/A	N/A	N/A
Animal drug	FFDCA § 512(j)	N/A	FFDCA § 564	N/A
Tobacco product	FFDCA § 910(g)	N/A	N/A	N/A
Biological product	FFDCA § 505(i)	FFDCA § 561	FFDCA § 564	FFDCA § 561B
Combination product	Depends on primary mode of action: FFDCA § 505(i) if drug or biologic PMOA; FFDCA § 520(g) if device PMOA	**	***	N/A

* As no marketing authorization is required for foods, cosmetics, dietary supplements, human tissues, HCT/Ps regulated solely under PHSA § 361, 42 U.S.C. § 264 (i.e., HCT/Ps not also regulated as drugs, devices, or combination products), and radiation-emitting products, those items are not listed on this chart.

** The main expanded access provision of the FFDCA neither expressly addresses nor expressly excludes combination products. *See* FFDCA § 561, 21 U.S.C. § 360bbb (setting out provisions for expanded access). However, it does authorize expanded access for each of the product categories that can be constituent parts of combination products (drugs, biologics, and devices). *Id.* This may leave some room for the FDA to determine, via rulemaking or guidance, whether—and, if so, to what extent—expanded access is available for combination products.

*** The main emergency use provision of the FFDCA neither expressly addresses nor expressly excludes combination products. *See* FFDCA § 564, 21 U.S.C. § 360bbb-3 (setting out provisions for emergency use). However, it does authorize emergency use for each of the product categories that can be constituent parts of combination products (drugs, biologics, and devices). *Id.* This may leave some room for the FDA to determine, via rulemaking or guidance, whether—and, if so, to what extent—emergency use authorization is available for combination products.

Appendix D: Claims-Authorization Processes for Food and Dietary Supplements Chart

Figure 6:

CLAIMS AUTHORIZATION PROCESSES FOR FOOD AND DIETARY SUPPLEMENTS		
Product Category	**Type of Claim**	**Authorization Process**
Food	SSA health claim	Health claim petition under 21 C.F.R. § 101.70
	Qualified health claim	Qualified health claim petition under May 2006 Guidance
	Nutrient content claim	Nutrient content claim petition under 21 C.F.R. § 101.69
Dietary supplement	SSA health claim	Health claim petition under 21 C.F.R. § 101.70
	Qualified health claim	Qualified health claim petition under May 2006 Guidance
	Nutrient content claim	Nutrient content claim petition under 21 C.F.R. § 101.69
	Structure/function claim	Notification under 21 C.F.R. § 101.93