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The FDA's Power Over Non-Therapeutic Uses of Drugs and Devices

Patricia J. Zettler

The Ohio State University, zettler.25@osu.edu

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The FDA's Power Over Non-Therapeutic Uses of Drugs and Devices

Patricia J. Zettler*

Abstract

Although we often—and rightly—think of the U.S. Food and Drug Administration (FDA) as regulating important therapies for patients, the agency also can regulate non-therapeutic uses of drugs and devices. The Federal Food, Drug, and Cosmetic Act defines drugs and devices as including not only products intended to address disease but also those intended to affect the structure or function of the body, such as cognitive enhancements, wrinkle removers, and recreational drugs. Indeed, if these broad definitions were read literally, many everyday consumer products—such as winter jackets intended to

* Patricia J. Zettler is an associate professor at The Ohio State University Moritz College of Law and a member of Ohio State's Comprehensive Cancer Center and its Drug Enforcement and Policy Center. For helpful discussion and comments, the author thanks Greer Donley, Tabrez Ebrahim, Hank Greely, Sam Halabi, Matt Lamkin, Erika Lietzan, Aisling McMahon, Laura Pedraz-Fariña, Govind Persad, Nicholson Price, Anya Prince, Ana Rustchman Santos, Rachel Sachs, Jake Sherkow, Helen Yu, and participants in the Research Roundtable and Conference on Permits, Licenses, and the Administrative State at the C. Boyden Gray Center for the Study of the Administrative State at George Mason University's Antonin Scalia Law School, the Wiet Life Science Law Scholars Conference at Loyola University Chicago School of Law, the Stanford Law and the Biosciences Workshop, the FDA: Past, Present & Future Conference at American University Washington College of Law, the University of North Carolina School of Law Faculty Workshop, and the Regulation and Innovation in the Biosciences (RIBS) Workshop at University of Copenhagen's Centre for Advanced Studies in Biomedical Innovation Law. This project received support from the Gray Center for the Study of the Administrative State.

keep wearers' warm—may be drugs or devices. Accordingly, Congress, courts, and the agency itself have sought reasonable limits on the definitions.

This Article critiques one limit that is sometimes offered: that the FDA cannot regulate certain non-therapeutic technologies because those technologies cannot be shown to be safe and effective. A careful review of the FDA's past decisions on non-therapeutic uses reveals that this reasoning is descriptively incorrect. Further, examining the purposes of FDA oversight demonstrates that the agency is not necessarily normatively required to set an insurmountable bar for showing the safety and effectiveness of non-therapeutic uses. Reconsidering this reasoning as a limit on FDA jurisdiction is warranted at a time when evolutions in both policy and science are opening the door to a potentially diverse market of new, or newly legal, non-therapeutic technologies.

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INTRODUCTION

Each fall as Halloween approaches, stories of the dangers of costume contact lenses—lenses that change the consumer's eye color or give the appearance of, for example, cat or zombie eyes—saturate the media.¹ News reports tell of consumers who have contracted serious eye infections or suffered injuries, such

1. See, e.g., Robert Preidt, *Skip Costume Contact Lenses This Halloween*, U.S. NEWS (Oct. 25, 2020), <https://perma.cc/73LX-SDNY> (“Halloween is risky enough this year with the coronavirus pandemic, so don't risk your vision as well by wearing costume contact lenses, the American Academy of Ophthalmology (AAO) says.”); Austin Williams, *Woman Rushed to ER after Colored Contact Lenses She Bought at Store for Halloween Nearly Blind Her*, FOX 5 WASH. D.C. (Oct. 30, 2019), <https://perma.cc/YJW2-DH3P> (believing that the FDA authorized the non-prescription lenses she purchased, the woman wore the lenses for a week until her eyes began to “burn, turn red, and become extremely sensitive to light” due to corneal infection); Phillip Yuhas, *The Scariest Part of Halloween May Be the Costume Contact Lenses, an Eye Doctor Says*, CONVERSATION (Oct. 28, 2019, 9:09 AM), <https://perma.cc/9FLE-A5KY> (“Poorly fitting costume lenses can cause many eye problems, including surface abrasions, allergic reactions and blurred vision.”); Venessa Wong, *Those Colored Contact Lenses Can Seriously Damage Your Eyes and People Are Worried*, BUZZFEED (Nov. 1, 2017, 5:32 PM), <https://perma.cc/4MM7-CBXY> (warning individuals “of the hazards and the strong possibility of permanent eye damage—including blindness—from wearing over-the-counter colored contact lenses that are increasingly popular among children and teens who want to dress up as zombies, that are now on sale on-line and at many retail stores” (quoting Rebecca Seawright)).

as corneal tears, leading to years of medical treatment, surgeries, and for some, permanent damage to their vision.² A common theme is that the injured consumers believed that the lenses were safe because they believed that the U.S. Food and Drug Administration (FDA) had evaluated the lenses.³

In many ways, this belief makes sense. Notwithstanding the fact that costume lenses have no therapeutic value—they do not correct sight or address disease in any way—they pose the same risks as contact lenses that correct the wearer’s vision and that are commonly understood to be devices subject to FDA oversight.⁴ Indeed, the FDA *does* regulate all contact lenses, regardless of whether they are corrective or decorative, as devices that require premarket authorization from the agency.⁵

Decorative contact lenses, thus, help to illustrate the reach of FDA authority. Although discussions of FDA regulation of drugs and devices often—and, particularly amid the COVID-19 pandemic, understandably—focus on the agency’s oversight of

2. See, e.g., Williams, *supra* note 1 (“Gaye was lucky. In most cases, an infection from a scraped cornea requires a corneal transplant in order to restore vision. In some extreme cases, permanent blindness can occur.”).

3. See *id.* (stating that many people buy such lenses from gas stations and costume shops that sell them illegally).

4. See U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY, FDA STAFF, EYE CARE PROFESSIONALS, AND CONSUMERS: DECORATIVE, NON-CORRECTIVE CONTACT LENSES 2 (2006), <https://perma.cc/C2P5-PRKP> (PDF) [hereinafter DECORATIVE LENSES GUIDANCE].

5. See 21 U.S.C. § 360j(n) (“All contact lenses shall be deemed to be devices”); DECORATIVE LENSES GUIDANCE, *supra* note 4, at 3 (“Although FDA had taken the position that contact lenses intended solely for decorative use may be regulated as cosmetics under section 201(i) of the Act, enactment of section 520(n) requires that all contact lenses be regulated as devices.”). Many of the news reports of injuries, however, appear to have involved decorative lenses that did not go through the required FDA premarket authorization process and were sold illegally without a prescription. See, e.g., Williams, *supra* note 1. For a fuller discussion of how the FDA came to regulate all contact lenses, see *infra* Part II.B.

important therapies,⁶ the FDA's jurisdiction also can extend to non-therapeutic uses of drugs and devices.⁷

This is generally because the Federal Food, Drug, and Cosmetic Act⁸ (FDCA) broadly defines “drugs”⁹ and “devices” to include not only products intended to address disease, but also products “intended to affect the structure or any function of the body.”¹⁰ Consistent with this statutory language, the FDA's drug and device authorities have been applied to a wide range of non-therapeutic technologies including products intended to enhance the cognitive or athletic performance of healthy individuals, breast implants for aesthetic augmentation, and

6. For example, the long-standing debate about terminally and seriously ill patients' pre-approval access to experimental interventions focuses not just on the FDA's role in regulating therapeutic products, but on that role in the context of therapeutic products intended for very sick patients who lack good treatment options. See, e.g., Lewis A. Grossman, *AIDS Activists, FDA Regulation, and the Amendment of America's Drug Constitution*, 42 AM. J.L. & MED. 687, 721 (2016); cf. Barbara J. Evans & Ellen Wright Clayton, *Deadly Delay: The FDA's Role in America's Covid-Testing Debacle*, 130 YALE L.J.F. 78, 78–79 (2020) (analyzing the FDA's role in regulating COVID-19 testing).

7. See, e.g., Rebecca S. Dresser, Wendy E. Wagner & Paul C. Giannelli, *Breast Implants Revisited: Beyond Science on Trial*, 1997 WIS. L. REV. 705, 709 (noting that “in roughly 80 percent of cases” silicone breast implants are used solely for aesthetic purposes).

8. Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301–399i).

9. Certain products that are drugs under the FDCA—including vaccines, viruses, proteins, therapeutic serums, and analogous products—also meet the definition of a “biological product” under the Public Health Service Act. See 42 U.S.C. § 262(i); Public Health Services Act, Pub. L. No. 78–410, 58 Stat. 682 (1944) (codified as amended at 42 U.S.C. §§ 201–300mm-61). For example, gene therapies are both biological products and drugs. Although biological drug products and traditional small molecule drugs can pose different regulatory problems, the differences are not relevant for this Article, and, importantly, the FDA generally expects both kinds of products to satisfy the same “safe and effective” standard for premarket authorization. See 42 U.S.C. § 262(a)(2)(C); *FDA 101: Regulating Biological Products*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/N2XJ-GVJT> (PDF) (last updated July 25, 2008). For simplicity, therefore, this Article uses the term “drug” to include both traditional small molecule drugs and biological products, focusing its discussion on the language in the FDCA.

10. 21 U.S.C. § 321(g)–(h).

drugs intended for recreational use.¹¹ At the same time, the expansive language of the drug and device definitions in the FDCA poses a line-drawing problem. As Justice Breyer wrote in his dissenting opinion in *FDA v. Brown & Williamson Tobacco Corporation*,¹² if the text of the definitions were “taken literally,” the FDA could be authorized to regulate many everyday consumer products that are intended to affect the structure or function of the body, “includ[ing] everything from room air conditioners to thermal pajamas.”¹³

Almost certainly, there is widespread agreement that the FDA cannot, and should not, regulate products like thermal pajamas.¹⁴ But the question remains of where the precise boundaries of the drug and device definitions lie, and that question may become increasingly important as new, or newly legal, markets of non-therapeutic products, such as adult-use cannabis, emerge and potentially intersect with FDA jurisdiction.¹⁵ At times, Congress has stepped in to answer such

11. See, e.g., *United States v. Travia*, 180 F. Supp. 2d 115, 119 (D.D.C. 2001); Warning Letter from Michael Dutcher, Dir., FDA Minneapolis Dist., to Timothy Meyer, ALV Supplement Direct (Mar. 3, 2016), <https://perma.cc/KFU6-SSGG>; *Regulatory History of Breast Implants in the U.S.*, U.S. FOOD & DRUG ADMIN. (Feb. 8, 2019), <https://perma.cc/5E99-GVZM> (PDF).

12. 529 U.S. 120 (2000).

13. *Id.* at 168 (Breyer, J., dissenting); cf. ANTONIN SCALIA & BRYAN A. GARNER, *READING LAW: THE INTERPRETATION OF LEGAL TEXTS* 56 (2012) (“The words of a governing text are of paramount concern . . .”).

14. Cf. *Brown & Williamson Tobacco Corp.*, 529 U.S. at 168 (Breyer, J., dissenting) (“[It] may well be right that the statute should not be read to cover room air conditioners and winter underwear.”). But cf. Lars Noah, *Time to Bite the Bullet?: How an Emboldened FDA Could Take Aim at the Firearms Industry*, 53 CONN. L. REV. (forthcoming June 2021) (manuscript at i) ([T]he U.S. Food and Drug Administration (FDA) could try to use its ‘device’ authority to rein in companies that manufacture firearms”).

15. See, e.g., Sam Kamin, *Legal Cannabis in the U.S.: Not Whether but How?*, 50 U.C. DAVIS L. REV. 617, 623 (2016) (describing states’ adult-use cannabis initiatives); see also NAT’L ACADS. OF SCIS., ENG’G & MED., *HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE* 137 (2017) (describing the potential enhancement uses of genome editing technologies); Antonio Regalado, *Elon Musk’s Neuralink Is Neuroscience Theater*, MIT TECH. REV. (Aug. 30, 2020), <https://perma.cc/TYS7-6LA4> (quoting Elon Musk as describing the neurotechnology being developed by his company, Neuralink, as a “Fitbit in your skull”); cf. Alexis Lazzeri, *California Cannabis Regulations*

definitional questions by amending the FDCA for specific technologies, as it did in 2005 when it specified that all contact lenses, whether decorative or corrective, are devices.¹⁶ In many instances, however, the agency and courts are left to determine the boundaries of the definitions. One argument that has been a powerful tool for limiting the reach of the definitions—including in the Supreme Court majority opinion's analysis of FDA authority to regulate tobacco products as drug-delivery devices in *Brown & Williamson*—is that the FDA cannot regulate certain non-therapeutic technologies as drugs and devices because it would be impossible for those technologies to meet the FDCA's safety and effectiveness standards for premarket authorization.¹⁷

This Article calls for skepticism about, if not the demise of, that line of reasoning for at least two reasons. First, for better or worse,¹⁸ the FDA currently possesses, and has exercised, tremendous flexibility in how it interprets and implements its premarket authorization authorities. Consistent with this flexibility, a careful review of past FDA actions on non-therapeutic uses of drugs and devices reveals that FDA premarket authorization processes are not an insurmountable

and the Federal Food, Drug & Cosmetic Act: A Product Liability Perspective of Edible Cannabis, 16 HASTINGS BUS. L.J. 65, 73–74 (2020) (arguing that FDA could regulate cannabis edibles, whether intended for medical or adult use, under its food authorities).

16. See 21 U.S.C. § 360j(n); DECORATIVE LENSES GUIDANCE, *supra* note 4, at 3.

17. See *Brown & Williamson Tobacco Corp.*, 529 U.S. at 143; see also *Whether the Food and Drug Administration Has Jurisdiction over Articles Intended for Use in Lawful Executions*, 43 Op. O.L.C. 1, 1–2 (2019) [hereinafter 2019 OLC Memo], <https://perma.cc/HU3J-ZW83> (concluding that substances used in executions are within FDA jurisdiction partly because FDA regulation “would effectively require their prohibition”). For the statutory standards related to safety and effectiveness, see, for example, 21 U.S.C. § 355(d); *id.* § 360c(f)(2); *id.* § 360c(i); *id.* § 360e(d); 42 U.S.C. § 262(a).

18. Cf. Joshua D. Wallach, Joseph S. Ross & Huseyin Naci, *The US Food and Drug Administration's Expedited Approval Programs: Evidentiary Standards, Regulatory Trade-offs, and Potential Improvements*, 15 CLINICAL TRIALS 219, 220 (2018) (assessing potential problems with “flexible approval standards”).

obstacle to marketing.¹⁹ Returning to the example of decorative contact lenses, they, like corrective lenses, are associated with serious (albeit relatively rare) risks like blindness, and transient, purely aesthetic, and undoubtedly to some, trivial, benefits.²⁰ Nevertheless, they have received FDA authorization.

Second, considering the purposes of FDA premarket authorization, including both protecting the public from harmful or ineffective products and forcing the development of information needed to understand the effects of drugs and devices,²¹ the conclusion that the FDA cannot determine

19. See *infra* Part III.B.

20. See DECORATIVE LENSES GUIDANCE, *supra* note 4, at 2 (enumerating the risks of decorative lenses including blindness, infection, corneal scarring, and even loss of the eye).

21. See, e.g., U.S. FOOD & DRUG ADMIN., MEMORANDUM: PUBLIC HEALTH INTERESTS AND FIRST AMENDMENT CONSIDERATIONS RELATED TO MANUFACTURER COMMUNICATIONS REGARDING UNAPPROVED USES OF APPROVED OR CLEARED MEDICAL PRODUCTS 4–10 (Jan. 2017) [hereinafter FDA MEMO], <https://perma.cc/7S8E-JCYP> (describing various ways FDA authorities advance public health); DANIEL CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA 16 (2010) (“[F]ederal regulation prevents and deters many sub-par and unsafe therapies from entering the American health-care system.”); Daniel Carpenter et al., *Approval Regulation and Endogenous Consumer Confidence: Theory and Analogies to Licensing, Safety, and Financial Regulation*, 4 REGUL. & GOVERNANCE 383, 400 (2010) (“Approval regulation leads to a superior distribution of products, . . . the provision of more information, and information of a higher quality”); Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. TECH. L. REV. 345, 347 (2007) (emphasizing the “important structural role that drug regulation has come to play in promoting a valuable form of pharmaceutical innovation”) [hereinafter Eisenberg, *The Role of the FDA in Innovation Policy*]; Rebecca S. Eisenberg, *The Problem of New Uses*, 5 YALE J. HEALTH POL’Y L. & ETHICS 717, 719–20 (2005) (asserting that the FDA motivates investment in clinical trials—leading to greater information regarding a given drug and its effects—is by requiring trials for approval); Amy Kapczynski, *Dangerous Times: The FDA’s Role in Information Production, Past and Future*, 102 MINN. L. REV. 2357, 2358 (2018) (“The core function of the FDA as a drug regulator . . . is not to make choices for the public, or to certify the truth, but to generate and validate information about medicines.”); Christopher Robertson & Victor Laurion, *Tip of the Iceberg II: How the Intended-Uses Principle Produces Medical Knowledge and Protects Liberty*, 11 N.Y.U. J.L. & LIBERTY 770, 774 (2017) (“By putting the burden of proof on drug and device makers who typically hold patents, and thus can reap the profits from proven

non-therapeutic uses to be safe and effective may not be required as a normative matter. For example, the FDA reasonably could view consumers—who voluntarily elect to use products for non-therapeutic purposes—as in need of less protection than patients, who may be de facto forced to use a drug or device by their disease or condition.²² Such a view may justify a flexible approach to weighing a non-therapeutic product's benefits and risks.²³ To be clear, this is not to say that the FDA will, or must, conclude that all non-therapeutic uses are safe and effective (or that all non-therapeutic technologies fall within its jurisdiction).²⁴ Rather, this Article argues that the FDCA does not preclude the agency from evaluating the safety and effectiveness of specific non-therapeutic uses, just as it evaluates therapeutic ones, without necessarily banning entire categories of technologies.

To develop the Article's arguments, Part I first describes what this Article means by the term "non-therapeutic use," and how such uses could fall within the drug and device definitions. Part II examines some boundaries on the expansive drug and device definitions, and explains why the argument that non-therapeutic uses could never be judged safe and effective may be a tempting tool to limit FDA jurisdiction. Part III explains the flexibility that the FDCA gives the agency to determine when a use is safe effective. It then considers the

uses, [the FDCA] regulatory regime produces knowledge which was not produced in the unregulated market that preceded it.”).

22. Cf. Patricia J. Zettler, *What Lies Ahead for FDA Regulation of tDCS Products?*, 3 J.L. & BIOSCIENCES 318, 322 (2016) [hereinafter *What Lies Ahead*] (“[W]e might think that individuals who are sick deserve special protection from unproven or risky products and, therefore, less favorable or less certain risk-benefit profiles are acceptable for enhancement products that consumers voluntarily decide to use.”); Scott Gottlieb, Comm’r Food & Drugs, U.S. Food & Drug Admin., Speech at America’s Health Insurance Plans’ National Health Policy Conference: Capturing the Benefits of Competition for Patients (Mar. 7, 2018), <https://perma.cc/BQ22-FSY7> (“Is a patient really in a position to make an economically-based decision? . . . Of course not.”).

23. See *infra* notes 235–238 and accompanying text.

24. But see Maxwell J. Mehlman, *How Will We Regulate Genetic Enhancement?*, 34 WAKE FOREST L. REV. 671, 701 (1999) (arguing that the FDA’s assessment of the safety and effectiveness of non-therapeutic technologies “would be compromised by the data deficiencies and subjectivity of judgments about risk and benefit”).

FDA's history of assessing the risks and benefits of non-therapeutic uses of drugs and devices, demonstrating that the agency's premarket review, as a descriptive matter, has not been an insurmountable obstacle. Finally, Part IV begins to examine how the FDCA's safety and effectiveness standard should be applied to non-therapeutic uses, in light of the purposes that FDA premarket review of safety and effectiveness is thought to serve. At a time when new, or newly legal, non-therapeutic technologies may be poised to emerge, better understanding of the potential scope of FDA jurisdiction is critical to anticipating the regulatory landscape for such technologies.

I. NON-THERAPEUTIC USES AND THE DRUG AND DEVICE DEFINITIONS

The line between therapeutic, and non-therapeutic technologies, is, as numerous scholars have noted, difficult to draw.²⁵ Moreover, the FDA does not formally distinguish between therapeutic and non-therapeutic uses of products that meet the definition of a drug or device—a drug is a drug, and a device is a device, whether or not its purpose is therapeutic. The FDA generally has jurisdiction over any product that falls within these definitions.²⁶ This Part, thus, starts by describing

25. See, e.g., Henry T. Greely, *Direct Brain Interventions to Treat Disfavored Human Behaviors: Ethical and Social Issues*, 91 CLINICAL PHARMACOLOGY & THERAPEUTICS 163, 163 (2012) (“Behaviors do not come naturally labeled as ‘disease’ and ‘nondisease;’ humans make those distinctions, and . . . we regularly change them . . .”); Matt Lamkin, *Legitimate Medicine in the Age of Consumerism*, 53 U.C. DAVIS L. REV. 385, 421 (2019) [hereinafter *Legitimate Medicine*] (describing “the blurring line between medical and recreational [drug] use”).

26. To be within the FDA's jurisdiction, a product both must meet the definition of a drug or device and it (or one of its components) must move in interstate commerce. See 21 U.S.C. § 321(g)(1); *id.* § 321(h); *id.* § 331. However, because modern supply chains and production processes generally involve at least one component of a product crossing state or national boundaries, this latter limitation on the FDA's jurisdiction is rarely relevant. Cf. *United States v. Regenerative Scis., LLC*, 741 F.3d 1314, 1320 (D.C. Cir. 2014) (finding the required intersection with interstate commerce for an autologous stem cell intervention); Memorandum from Robert Charrow, Gen.

what this Article means by the term “non-therapeutic use” of a drug or device, in the absence of an FDA definition. It then explains how such non-therapeutic uses can fit within the FDCA’s drug and device definitions.

A. *Defining ‘Non-Therapeutic Uses’*

To start, this Article generally uses the term non-therapeutic *use*, rather than non-therapeutic *product*, because the FDA’s regulatory scheme addresses specific uses of products.²⁷ Regardless of a drug or device’s route through the

Couns., Dep’t Health & Hum. Servs. to Stephen Hahn, Comm’r Food & Drugs 7 (June 22, 2020) [hereinafter LDT Memo], <https://perma.cc/5UTK-L7AV> (PDF) (explaining the interstate commerce requirement for devices in the FDCA). Jurisdictional debates also arise over whether a particular intervention—for example, a stem cell intervention—involves a product regulated by the FDA or is, instead, a part of medical practice, typically thought to be regulated by the states. See *Regenerative Scis.*, 741 F.3d at 1319–20. As I have argued elsewhere, the product-practice distinction, however, is blurry and may not be useful for determining the scope of the FDA’s jurisdiction. See Patricia J. Zettler, *Pharmaceutical Federalism*, 92 IND. L.J. 845, 892 (2017); see also Lars Noah, *Ambivalent Commitments to Federalism in Controlling the Practice of Medicine*, 53 U. KAN. L. REV. 149, 173 (2004) (“Given its power to prevent the sale of drugs and medical devices until persuaded of their safety and effectiveness, the FDA undoubtedly affects the practice of medicine, even if only indirectly.”); Barbara J. Evans, *Distinguishing Product and Practice Regulation in Personalized Medicine*, 81 CLINICAL PHARMACOLOGY & THERAPEUTICS 288, 288 (2007) (“[P]reserving the crucial distinction between product and practice regulation, may require innovative regulatory approaches”); Margaret Foster Riley, *An Unfulfilled Promise: Changes Needed to the Drug Approval Process to Make Personalized Medicine a Reality*, 70 FOOD & DRUG L.J. 289, 308 (2015) (“In 2007, FDAAA introduced potentially far-reaching limits on the practice of medicine doctrine allowing FDA to impose restrictions (e.g. place and mode of use) on approved drugs”); Myrisha S. Lewis, *How Subterranean Regulation Hinders Innovation in Assisted Reproductive Technology*, 39 CARDOZO L. REV. 1239, 1265 (2018) (“In light of the blurring distinctions between medical devices, human tissues, drugs, and the practice of medicine, if the FDA does have jurisdiction over advanced assisted reproductive technologies, it should clearly explain the source of that jurisdiction”); Myrisha S. Lewis, *Innovating Federalism in the Life Sciences*, 92 TEMP. L. REV. 383, 391 (2020) (explaining that the line between medical practice and medical products “has been ‘blurring’ over time”).

27. See, e.g., FDA MEMO, *supra* note 21, at 1.

FDA's premarket review processes, an FDA authorization decision is specific to the product's intended use.²⁸ That is, the FDA does not assess a product's safety and effectiveness as a general matter. Rather it assesses the benefits and risks for the specific use described in the product's proposed labeling. Accordingly, the FDA might judge the exact same product to be safe and effective for one use but not for another. For example, in 2004 the FDA approved the drug Avastin (bevacizumab) for treating colon cancer, and then in subsequent years for use in breast, lung, kidney, and brain cancers as well.²⁹ In 2011, the FDA withdrew its approval of Avastin for use in metastatic breast cancer after determining the drug had not been demonstrated safe and effective for that one use.³⁰ The drug, however, remains approved for the other uses, for which, in the FDA's view, there continues to be evidence that the drug's benefits outweigh its risks.³¹

Perhaps more relevant, however, is the question of what this Article means by "non-therapeutic." Although some of the limits on the FDA's drug or device jurisdiction implicate the line between therapeutic and non-therapeutic uses of products, the FDA has not formally explained—such as through guidance or a regulation—the agency's thinking about what constitutes a therapeutic or a non-therapeutic use of a drug or device.³² In the

28. See 21 U.S.C. § 355(d); *id.* § 360c(f)(2); *id.* § 360c(i); *id.* § 360e(d); 42 U.S.C. § 262(a); *see also* FDA MEMO, *supra* note 21, at 1 (describing the reasons for evaluating a product for a particular use).

29. See, e.g., *Summary Review for Regulatory Action: Avastin*, U.S. FOOD & DRUG ADMIN. (Aug. 14, 2014), <https://perma.cc/VKV3-4CGU> (PDF).

30. See *Avastin (bevacizumab) Information*, U.S. FOOD & DRUG ADMIN. (Feb. 5, 2018), <https://perma.cc/G5DG-VVRS>.

31. See U.S. FOOD & DRUG ADMIN., *AVASTIN LABELING* (2020), <https://perma.cc/43HW-D2YU> (PDF).

32. For example, the FDA has declined to consider some device-like products that lack a medical purpose—such as certain exercise equipment—to be devices. See 21 C.F.R. § 890.5350 (2020); *see also* Physical Medicine Devices; General Provisions and Classification of 82 Devices, 48 Fed. Reg. 53,032, 53,035 (Nov. 23, 1983) (to be codified at 21 C.F.R. pt. 890) ("FDA has changed the regulations classifying many physical medicine devices to clarify that the regulations apply only to those products intended for medical purposes."). As another example, an agency regulation explains what constitutes a claim that a product affects the structure or function of the body

absence of an FDA definition and consistent with the literature,³³ this Article uses the term “non-therapeutic use” to describe aesthetic, enhancing, or recreational uses of drugs and devices, rather than health-maintenance or disease-addressing uses.³⁴

More specifically, aesthetic uses are those intended to alter a person's appearance in some way that affects the structure or function of the body, for example injecting human skin with a fluorescent protein from jellyfish to make the skin glow.³⁵ Enhancing uses are those intended to improve a healthy person's physical or mental performance to a level beyond what is typical for them or beyond the statistically normal range for humans.³⁶ For instance, students who use stimulants in an

versus a claim that a product addresses disease—because the line between such claims is critical to appropriately classifying certain products as either dietary supplements or drugs under the FDCA. See 21 C.F.R. § 101.93 (2020). But the line between a product use that is intended to affect the structure or function of the body and one that is intended to address disease is not necessarily the same as the line between a therapeutic and non-therapeutic use of that product. Some structure/function uses may be therapeutic. For example, “maintains healthy lung function” is a claim that a product is intended to affect the structure or function of the body, but such a claim also seems to have health-related implications—even if related to maintaining health rather than treating a deficit. Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, 65 Fed. Reg. 1,000, 1,018 (Jan. 6, 2000) (to be codified at 21 C.F.R. pt. 101). See *infra* Part II.B for further discussion of this point.

33. See, e.g., Henry T. Greely et al., *Towards Responsible Use of Cognitive-Enhancing Drugs by the Healthy*, 456 NATURE 702, 703 (2008).

34. Cf. Christi J. Guerrini et al., *DIY CRISPR*, 97 N.C. L. REV. 1399, 1413 (2019) (describing similar categories).

35. See Kristen V. Brown, *Genetically Engineering Yourself Sounds Like a Horrible Idea—But This Guy Is Doing It Anyway*, GIZMODO (Nov. 29, 2017, 10:00 AM), <https://perma.cc/82R5-TQQB> (describing a biohacker's attempt to make his skin glow).

36. See, e.g., 2 PRESIDENTIAL COMM'N FOR THE STUDY OF BIOETHICAL ISSUES, GRAY MATTERS: TOPICS AT THE INTERSECTION OF NEUROSCIENCE, ETHICS, AND SOCIETY 28 (2015) [hereinafter GRAY MATTERS], <https://perma.cc/33MA-36HW>; see also Henry T. Greely, *Remarks on Human Biological Enhancement*, 56 U. KAN. L. REV. 1139, 1140 (2008) (“[Enhancement] is using things not only to repair or bring up the human norm, but also to surpass either the preexisting position or to go to the extreme—to move outside the normal human range.”); Dov Fox, *Safety, Efficacy, and Authenticity: The Gap*

effort to improve their academic performance are often described as using drugs for cognitive enhancement.³⁷ Recreational uses are those uses of drugs and devices that are, perhaps most simply, not for therapeutic, aesthetic, or enhancing purposes.³⁸ Inhaling nitrous oxide for a high, for instance, would be a recreational or adult use.³⁹

Of course, where to draw the line between an aesthetic, enhancing, recreational, or therapeutic use is not always, and perhaps is only rarely, clear.⁴⁰ For example, a leading advocate for legalizing medical uses of cannabis famously asserted that “all [adult] marijuana use is medical”—on the ground that “stress relief is a medical purpose, [so] any adult who uses cannabis does so for medical reasons.”⁴¹ As another example, people who use attention deficit hyperactivity disorder (ADHD)

Between Ethics and Law in FDA Decisionmaking, 2005 MICH. ST. L. REV. 1135, 1137–38 (“Enhancements are distinct from other biomedical products in that they are put to uses which extend beyond the goal of preventing disease, repairing disability, and restoring physiological wholeness.”); cf. Efthimios Parasidis, *Human Enhancement and Experimental Research in the Military*, 44 CONN. L. REV. 1117, 1129 (2012) (explaining that the military has “sought to leverage innovative medical products and technologies . . . to make the individual warfighter stronger, more alert, more enduring, and better able to heal” (internal quotations omitted)).

37. See Greely et al., *supra* note 33, at 702; see also *Legitimate Medicine*, *supra* note 25, at 422 (discussing the difficulty of distinguishing medical and enhancing uses of certain drugs).

38. Cf. Kamin, *supra* note 15, at 623–24 (“Recreational laws short-circuit the entire rubric of the [Controlled Substances Act] framework, treating marijuana not as a controlled substance at all, but as something more akin to alcohol or tobacco.”).

39. See, e.g., Aaron Rowe, *Chem Lab: The Downside of Getting High on Nitrous Oxide*, WIRED (Dec. 9, 2007, 9:49 PM), <https://perma.cc/64NC-NCL8>.

40. See, e.g., GRAY MATTERS, *supra* note 36, at 28–29 (“Drawing clear lines between *maintaining or improving* function within normal ranges on one hand and *expanding or augmenting* on the other, or between *treating* as therapy on one hand and *expanding or augmenting* as enhancement on the other, can be difficult in both theory and practice.”); *Legitimate Medicine*, *supra* note 25, at 387 (describing the “[c]ommon . . . confusion regarding the scope of legitimate medicine and the nature of drug abuse” that permeates controversies over use of various drugs).

41. Lewis A. Grossman, *Life, Liberty, [and the Pursuit of Happiness]: Medical Marijuana Regulation in Historical Context*, 74 FOOD & DRUG L.J. 280, 282–83 (2019) (quoting Dennis Peron).

drugs to enhance their cognitive performance describe their reasons for doing so similarly to how patients who are prescribed drugs to treat their ADHD describe their reasons for use.⁴² Partly for this reason, Matt Lamkin has argued that such enhancing uses are distinguishable from therapeutic uses only “by whether the user has a prescription for the drug.”⁴³

Not only is the distinction between therapeutic and non-therapeutic uses a conceptually hazy one, but the pharmaceutical and device industries also have long been criticized for proactively muddying the distinction to help sell their products.⁴⁴ Critics argue that some industry advertising and promotion efforts medicalize the discomforts of ordinary life to sell more products—such as a disease awareness campaign that seeks to persuade consumers that particular symptoms might constitute the treatable condition of “overactive bladder.”⁴⁵ Similarly, certain business models may blur the line between therapeutic and non-therapeutic uses, as with at-home teeth aligners that are marketed as providing aesthetic improvements to users’ smiles but also as products that may be eligible for dental insurance coverage.⁴⁶

Questions about what counts as therapeutic and non-therapeutic uses—and how the distinction between the two might be manipulated—are important. But they are not the focus of this Article. Instead, this Article aims to consider the FDA’s jurisdiction over non-therapeutic uses of drugs and devices, whatever may fall into that “non-therapeutic” category. For that reason, this Article focuses on examples of drug and device uses that are generally, albeit not always, agreed to be non-therapeutic, such as the use of Botox (onabotulinumtoxinA)

42. See *Legitimate Medicine*, *supra* note 25, at 421–23.

43. *Id.* at 422.

44. See, e.g., Ray Moynihan et al., *Selling Sickness: The Pharmaceutical Industry and Disease Mongering*, 324 *BRIT. MED. J.* 886, 887 (2002).

45. See, e.g., *id.* at 889.

46. See, e.g., SMILE DIRECT CLUB, <https://perma.cc/KL53-MCPV>; cf. Anna Wexler et al., *Direct-to-Consumer Orthodontics: Surveying User Experience*, 151 *J. AM. DENTAL ASSOC.* 625, 634 (2020) (describing consumers as having both aesthetic and oral-health-related reasons for seeking at-home teeth aligners).

to reduce facial wrinkles, the use of decorative contact lenses to change the appearance of the users' eyes, and the recreational use of substances. Such uses of drugs and devices, also, notably, are not generally covered by health insurance plans, which typically reimburse for "medically necessary" services.⁴⁷

B. *The Expansive Text of the Statutory Definitions*

However precisely defined, non-therapeutic uses can fall within the FDA's drug and device jurisdiction. The FDCA defines drugs and devices as including articles "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" and those "intended to affect the structure or any function of the body."⁴⁸ It is this latter part of the definition that generally has enabled the FDA to assert that non-therapeutic uses fall within its drug and device authorities.

Given this statutory language, the key for determining whether an "article" is a drug or a device is typically its "intended use."⁴⁹ FDA regulations define intended use as the "objective intent of the persons legally responsible for the labeling," which is usually a product's manufacturer or seller.⁵⁰

47. "Medically necessary" is broad enough to include uses of drugs and devices that are health-related, but not disease-focused—such as pregnancy tests performed in a physician's office or oral contraceptives. *See, e.g.*, *EEOC v. United Parcel Serv., Inc.*, 141 F. Supp. 2d 1216, 1219 (D. Minn. 2001). However, "medically necessary" is not so broad as to typically include aesthetic, enhancing, or recreational uses of drugs and devices. *See, e.g., id.* at 1219 n.2.

48. 21 U.S.C. § 321(g)(1); *see id.* § 321(h) (defining "device"). Devices are distinguished from drugs largely by the kinds of items that they are—items that do not "achieve [their] primary intended purpose through chemical action within or on the body . . . and . . . [are] not dependent on being metabolized" to achieve that purpose. *Id.* § 321(h); *Genus Med. Techs., LLC v. FDA*, 427 F. Supp. 3d 74, 77 (D.D.C. 2019) (citing 21 U.S.C. § 321(h)). Additionally, devices, unlike drugs, include articles intended for use in the diagnosis of "conditions." 21 U.S.C. § 321(h); Shelby Baird, Note, *Don't Try This at Home: The FDA's Restrictive Regulation of Home-Testing Devices*, 67 *DUKE L.J.* 383, 393 (2017). This aspect of the device definition captures diagnostic tools that are not focused on diseases, but are nevertheless important, such as pregnancy tests. *See* 21 C.F.R. § 862.1155(a)(1) (2020).

49. *See* 21 C.F.R. §§ 201.128, 801.4 (2020).

50. *Id.* § 201.128.

Typically the requisite intended use is evinced by a manufacturer or seller's public statements suggesting, explicitly or implicitly, that a product is intended to address disease ("disease claims") or to affect the structure or function of the body ("structure/function claims").⁵¹ For example, a manufacturer might state in its drug labeling that the product is "indicated for the treatment of metastatic colorectal cancer," which would be a disease claim.⁵² As another example, a manufacturer might market a brain stimulation device for "increased [athletic] stamina and endurance,"⁵³ or as a way to "charge your mind," which would be explicit or implicit structure/function claims.⁵⁴

Consistent with these broad definitions, the FDA has asserted jurisdiction over a potentially surprising range of products. These include products commonly understood to be FDA-regulated drugs and devices, such as products marketed as cancer or COVID-19 therapies.⁵⁵ These also include some products that may not be commonly understood to fall within the FDA's drug and device authorities, such as antiperspirant,⁵⁶ epilators that remove hair,⁵⁷ and products intended to produce a "chill" similar to that produced by cannabis.⁵⁸

Further underscoring the expansiveness of the definitions is that a manufacturer or seller's public claims about its products are not the only source of evidence for ascertaining

51. See, e.g., *id.* § 101.93.

52. AVASTIN LABELING, *supra* note 31.

53. U.S. FOOD & DRUG ADMIN., Warning Letter to Big Dan's Fitness and Nutrition, LLC (May 25, 2017), <https://perma.cc/4Z8A-UMXV> (identifying "increased stamina and endurance" as a structure/function claim).

54. *What Lies Ahead*, *supra* note 22, at 318.

55. See AVASTIN LABELING, *supra* note 31; *COVID-19: An Update on the Federal Response: Hearing Before the S. Comm. on Health, Educ., Lab. & Pensions*, 116th Cong. 6 (2020).

56. See, e.g., PETER HUTT ET AL., *FOOD AND DRUG LAW: CASES AND MATERIALS* 117 (4th ed. 2013).

57. See 21 C.F.R. §§ 878.5350, 878.5360 (2020).

58. See U.S. FOOD & DRUG ADMIN., Warning Letter to Green Planet Inc. (Dec. 5, 2013), <https://perma.cc/4VB8-8QDF>.

intended use.⁵⁹ Courts have opined that the agency may consider “any relevant source” of evidence of intended use.⁶⁰ As recently as September 2020, in a rule proposing changes to the regulatory definition of intended use, the agency reaffirmed its own view that it may consider “any relevant source of evidence” to determine a product’s intended use.⁶¹ A product’s design,⁶² internal company statements,⁶³ statements that a company previously made but no longer makes,⁶⁴ and the overall

59. See 21 C.F.R. §§ 201.128, 801.4 (2020). For additional discussion of the kinds of evidence that may show a product’s intended use, see Patricia J. Zettler, et al., *Closing the Regulatory Gap for Synthetic Nicotine Products*, 59 B.C. L. REV. 1933, 1956–67 (2018).

60. See, e.g., *Nat’l Nutritional Foods Ass’n v. Mathews*, 557 F.2d 325, 334 (2d Cir. 1977); see also *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 143 (2000) (rejecting the FDA’s attempt to regulate tobacco products as drugs and devices, without disagreeing with the argument that the tobacco products’ design was evidence of their intended use).

61. Regulations Regarding “Intended Uses,” 85 Fed. Reg. 59,718, 59,721 (proposed Sept. 23, 2020) (to be codified at 21 C.F.R. pts. 201, 801).

62. See, e.g., *Nicotine in Cigarettes and Smokeless Tobacco Is a Drug and These Products Are Nicotine Delivery Devices Under the Federal Food, Drug, and Cosmetic Act: Jurisdictional Determination*, 61 Fed. Reg. 44,619, 44,636–37 (Aug. 28, 1996) (relying on product design as evidence of intended use); U.S. FOOD & DRUG ADMIN., *Warning Letter to Salton, Inc.* (Aug. 20, 2006), <https://perma.cc/327S-2YE3> [hereinafter *Rejuvenique Warning Letter*] (relying on the Rejuvenique product design as evidence of intended use).

63. See, e.g., *United States v. Vascular Sols., Inc.*, 181 F. Supp. 3d 342, 347 (W.D. Tex. 2016) (permitting the use of non-public statements as evidence of intended use).

64. See, e.g., *United States v. 789 Cases, More or Less, of Latex Surgeons’ Gloves, an Article of Device*, 799 F. Supp. 1275, 1285 (D.P.R. 1992) (“[A] manufacturer . . . cannot avoid the reaches of the [FDCA] by stating that the product has a different—and non-regulated use. The Courts have recognized the ‘carry-over effect’ that is created by a manufacturer’s original representations about the product.”); *United States v. Undetermined Quantities of an Article of Drug Labeled as “Exachol”*, 716 F. Supp. 787, 791 (S.D.N.Y. 1989) (“Courts have recognized that where years later customers purchase a product in reliance on the therapeutic claims of the previous literature marketed with that product, the court may use such literature to determine the intent in marketing the product despite a later disclaimer.”); see also *Allergan, Inc. v. Athena Cosms., Inc.*, 738 F.3d 1350, 1356–57 (Fed. Cir. 2013) (concluding that a company’s past claims that its product affected the structure of eyelashes were relevant to an intended use analysis because

environment in which a product is distributed⁶⁵ are all among the other kinds of evidence on which the FDA has relied to demonstrate the requisite intended use.⁶⁶ For instance, the FDA has taken the position that a machine designed to use electrical current to contract facial muscles, in order to tighten skin and reduce wrinkles, is a device “even if no claims were made for its specific use.”⁶⁷ In other words, a company cannot necessarily avoid its product being regulated as a drug or device solely by avoiding both disease and structure/function claims.

II. FINDING BOUNDARIES FOR THE DEFINITIONS

Although broad, the drug and device definitions are not limitless. Through the statutory structure of the FDCA or even through statutory amendments addressing specific technologies, Congress has placed boundaries on the scope of the drug and device definitions.⁶⁸ Likewise, courts and the FDA have sought to interpret the statute in ways that draw reasonable boundaries around the expansive definitions.⁶⁹ This section explores various boundaries on the drug and device definitions, and suggests that, for at least some emerging non-therapeutic uses, there is no clear limit on the FDA's ability to regulate them as drugs and devices⁷⁰ —leaving the door open

the company did not materially alter its product's formulation or disavow its previous claims).

65. See, e.g., *United States v. Storage Spaces Designated Nos. 8 & 49*, 777 F.2d 1363, 1366 n.5 (9th Cir. 1985) (concluding that the “overall circumstances” showed that products labeled as incense were drugs); *United States v. Travia*, 180 F. Supp. 2d 115, 119 (D.D.C. 2001) (concluding that unlabeled nitrous oxide sold outside a rock concert was a drug because the “environment provided the necessary information between buyer and seller”).

66. But see Sean M. O'Connor & Erika Lietzan, *The Surprising Reach of FDA Regulation of Cannabis, Even After Descheduling*, 68 AM. U. L. REV. 823, 903 (2019) (expressing skepticism about the FDA relying on these kinds of evidence of intended use).

67. Rejuvenique Warning Letter, *supra* note 62.

68. See *infra* Part II.A–B.

69. See *infra* Part II.C–E.

70. Cf. O'Connor & Lietzan, *supra* note 66, at 903 (arguing that the FDA asserting jurisdiction over recreational uses of cannabis products would be controversial).

to arguments that FDA cannot do so because the uses could never be judged safe and effective.

A. *Other Product Definitions*

One clear way that the drug and device definitions are limited are by the FDCA's definitions of "other products." Congress has placed certain kinds of non-therapeutic uses of products—that otherwise might satisfy the drug or device definition—outside the scope of the FDA's drug and device jurisdiction by creating other product categories, such as cosmetics,⁷¹ tobacco products,⁷² and dietary supplements.⁷³ Cosmetics are not intended to address disease or affect the structure or function of the body, and instead are intended "for cleansing, beautifying, promoting attractiveness, or altering . . . appearance."⁷⁴ Tobacco products—products "made or derived from tobacco" including e-cigarettes that use tobacco-derived e-liquid—cannot be marketed to address disease, but may be marketed as affecting the structure or function of the body as long as the structure/function claims are those that have been customarily made about tobacco (e.g., "satisfying").⁷⁵ Similarly, dietary supplements—which must

71. 21 U.S.C. § 321(i). A product can meet the definition of both a cosmetic and a drug or device, if it is intended to both alter appearance and affect the structure or function of the body. *See Is It a Cosmetic, a Drug, or Both? (Or Is It Soap?)*, U.S. FOOD & DRUG ADMIN. (Aug. 24, 2020), <https://perma.cc/Z3S9-FLSA>. In such instances of products that are a combination of a cosmetic and a drug or device, the product is regulated according to the more stringent drug or device rules. *See id.*

72. 21 U.S.C. § 321(ff). Unlike cosmetics, the FDA generally takes the position that a product cannot meet both the definition of a dietary supplement and of a drug or device, nor may a dietary supplement be combined with a drug or device. *See, e.g.*, U.S. FOOD & DRUG ADMIN., Warning Letter to Proctor & Gamble (Oct. 29, 2009), <https://perma.cc/YMR7-D7KA>.

73. 21 U.S.C. § 321(rr). The FDCA specifies that a product cannot meet both the definition of a tobacco product and of a drug or device, and that a tobacco product may not be combined with a drug or device. *See id.* § 321(rr)(2), (4).

74. *Id.* § 321(i).

75. *See id.* § 321(rr)(1); *Sottera, Inc. v. FDA*, 627 F.3d 891, 894 (D.C. Cir. 2010); *see also* Clarification of When Products Made or Derived from Tobacco

contain a dietary ingredient, such as an herb, and cannot contain approved or studied drug ingredients—generally may be marketed with structure/function claims but not disease claims.⁷⁶ Cosmetics and dietary supplements are generally not subject to FDA premarket review,⁷⁷ and, although new tobacco products are subject to premarket review, it is a different process than that for drugs and devices.⁷⁸ Through these avenues, therefore, some (but not all) products with non-therapeutic uses, such as a cosmetic cream intended to reduce the appearance of, but not the actual existence of, wrinkles or an herb intended to support muscle tone, may reach

Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding “Intended Uses,” 82 Fed. Reg. 2,193, 2,197–98 (Jan. 9, 2017) (to be codified at 21 C.F.R. pts. 201, 801, 1100) (noting that *Soterra* stands for the proposition that “customarily marketed tobacco products were sold without therapeutic claims and should be regulated as tobacco products under the [FDCA]”); *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 143 (2000) (concluding, before the Family Smoking Prevention and Tobacco Control Act of 2009 expressly granted the FDA authority to regulate tobacco products, that the FDA did not have authority to regulate tobacco products because they did not make claims about “therapeutic or medical benefit”); *Action on Smoking & Health v. Harris*, 655 F.2d 236, 240 (D.C. Cir. 1980) (affirming the FDA’s then-decision to decline to categorize cigarettes as drugs or devices). According to the FDA, a manufacturer’s claim that its tobacco product is “satisfying” is an implicit structure/function claim that amounts to a “euphemism[] for the delivery of a pharmacologically active dose of nicotine.” Clarification of When Products Made or Derived from Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding “Intended Uses,” 82 Fed. Reg. 2,204.

76. See 21 U.S.C. § 343(r)(6)(A); 21 C.F.R. §§ 101.14(a)(1), 101.93 (2020); see also *Label Claims for Conventional Foods and Dietary Supplements*, U.S. FOOD & DRUG ADMIN. (June 19, 2018), <https://perma.cc/ZM4A-AAVX> (explaining that in some circumstances, claims can be made that dietary supplements are intended to reduce the risk of disease—for example that calcium may reduce the risk of developing osteoarthritis—without triggering the FDA’s drug authorities).

77. See, e.g., *Is It a Cosmetic, a Drug, or Both? (Or Is It Soap?)*, *supra* note 71.

78. Compare 21 U.S.C. § 387j (providing the standard for premarket review of tobacco products), with *id.* § 355(d) (providing the approval standard for drugs).

the market without being subject to the FDA's drug and device requirements.⁷⁹

B. *Statutory Amendments for Specific Technologies*

Notwithstanding these other product categories, the broad language of the drug and device definitions generally gives the FDA wide discretion to determine what products are subject to drug and device requirements—discretion that the agency has used both to decline, and to assert, jurisdiction over certain non-therapeutic uses.⁸⁰ At times, when Congress has disagreed with the agency's decision about its jurisdiction, it has amended the FDCA to address whether a specific non-therapeutic technology is a drug or device.⁸¹

The story behind how FDA came to regulate decorative contact lenses as devices provides one example. In 2002, there were reports that the FDA was going to decline to categorize decorative lenses as devices.⁸² After learning this news, in August 2002, then-Representative Henry Waxman wrote a letter to then-Secretary of Health and Human Services Tommy Thompson arguing that all contact lenses are devices under the

79. See, e.g., Regulations on Statements Made for Dietary Supplements Concerning the Effect of the Product on the Structure or Function of the Body, 65 Fed. Reg. 1,000, 1,020 (Jan. 6, 2000) (to be codified at 21 C.F.R. pt. 101).

80. See, e.g., *Brown & Williamson Tobacco Corp.*, 529 U.S. at 126; *Harris*, 655 F.2d at 236.

81. Because the FDA is an agency within the Department of Health and Human Services (HHS), HHS also may overrule FDA decisions on product jurisdiction. In August 2020, HHS issued an announcement limiting the FDA's ability to regulate a category of diagnostic tests known as laboratory-developed tests (LDTs). See *Rescission of Guidances and Other Informal Issuances Concerning Premarket Review of Laboratory Developed Tests*, DEP'T OF HEALTH & HUM. SERVS. (Aug. 19, 2020), <https://perma.cc/B82T-7VUK>. Although LDTs may not have many, if any, non-therapeutic uses, the LDT story provides an example of how HHS can affect the FDA's flexibility to determine the scope of its jurisdiction. See LDT Memo, *supra* note 26, at 2 (stating that HHS is deciding “under what circumstances, if any, does [the] FDA have the jurisdiction to regulate LDTs”).

82. See *Proposal to Regulate Nonprescription Contact Lenses as Cosmetics Triggers Health Concerns*, 10 NO. 12 GUIDE MED. DEVICE REG. NEWSL. 4 (2002) (describing concerns among Congress members and eye care professionals as a result of these reports, and the letter from Rep. Waxman).

FDCA.⁸³ The letter asserted that “a contact lens . . . reduces the flow of oxygen to and carbon dioxide from the cornea, create[ing] pressure on the underlying tissues and reduces wetting of the ocular surface” and thus “[a]ny manufacturer . . . that intends for users to place the products in the eye must also intend for these [structure/function] effects to occur.”⁸⁴ Nevertheless, in 2003, the FDA opined that decorative contact lenses were cosmetics intended to beautify, and *not* devices, “[p]rovided they are not marketed with claims that they effect physical or physiological change.”⁸⁵ Ultimately, because of concerns about the risks of decorative lenses, in 2005, Congress removed the agency’s discretion on the issue and amended the FDCA to specify that all contact lenses are devices.⁸⁶

The FDA’s attempt to regulate certain mobile medical apps provides another example—but of Congress rejecting the agency’s attempt to assert, rather than decline, jurisdiction. In 2013, the FDA issued a guidance document explaining its approach to regulating mobile medical apps as devices.⁸⁷ Certain members of Congress then expressed concern that FDA oversight would stifle innovation. In 2016, Congress ultimately

83. *Id.*

84. *Id.*

85. Guidance for FDA Staff on Sampling or Detention Without Physical Examination of Decorative Contact Lenses (Import Alert #86-10); Availability, 68 Fed. Reg. 16,520, 16,521 (Apr. 4, 2003) [hereinafter 2003 Decorative Lenses Import Alert]; see 21 U.S.C. § 321(i) (defining cosmetic). The FDA similarly took the position that decorative lenses were cosmetics in an October 2002 Import Alert, but without explaining its reasoning. *Detention Without Physical Examination of Decorative Contact Lenses (Import Alert #86-10)*, U.S. FOOD & DRUG ADMIN. (Oct. 22, 2002), <https://perma.cc/RJG9-2ENR> (PDF). The agency reportedly adopted the new position on decorative lenses following a meeting between the agency’s then-Chief Counsel and a manufacturer of decorative contact lenses. See *Proposal to Regulate Nonprescription Contact Lenses as Cosmetics Triggers Health Concerns*, *supra* note 82.

86. See 21 U.S.C. § 360j(n); DECORATIVE LENSES GUIDANCE, *supra* note 4, at 2; *Decorative Lenses Catch Congress’s Eye*, 13 No. 11 GUIDE MED. DEVICE REG. NEWSL. 8 (2005).

87. See U.S. FOOD & DRUG ADMIN., POLICY FOR DEVICE SOFTWARE FUNCTIONS AND MOBILE MEDICAL APPLICATIONS 10 (2013), <https://perma.cc/EQA3-EP7X> (PDF) (describing the FDA’s regulatory approach for device software functions).

passed the 21st Century Cures Act, which, among other things, amended the FDCA to exclude from the device definition software—such as mobile apps—intended “for maintaining or encouraging a healthy lifestyle” when “unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition.”⁸⁸ Although “maintaining or encouraging a healthy lifestyle” may suggest that software falling into this non-device category must have a therapeutic, health-related purpose, the FDA has taken the position that this definition also encompasses enhancing uses, such as products intended to “enhance learning capacity.”⁸⁹ For example, a video game meant to improve a healthy person’s mental acuity—although intended to affect the structure or function of the brain—is likely no longer a device under the FDA’s jurisdiction.⁹⁰ Such software is now not just outside of the FDA’s drug and device authorities, but is completely outside the agency’s jurisdiction. Nevertheless, many non-therapeutic uses have not been specifically addressed by Congress in this manner and may remain within the drug and device definitions.

C. *Off-Label Uses*

Even when a particular product does fall within the drug or device definitions, the FDA, nevertheless, may not be tasked with reviewing and authorizing a non-therapeutic use of that product if the use is “off-label.” This is because, as explained in Part I.A, the agency’s weighing of the product’s risks and benefits, and its authorization decision, is not for a product as a

88. 21st Century Cures Act, Pub. L. No. 114-255, § 3060, 130 Stat. 1033, 1130 (2016). The concerns that FDA oversight would impede innovation in the mobile medical app industry were not necessarily justified. *See, e.g.*, Nathan G. Cortez et al., *FDA Regulation of Mobile Health Technologies*, 371 NEW ENG. J. MED. 372, 373–75 (2014).

89. U.S. FOOD & DRUG ADMIN., GENERAL WELLNESS: POLICY FOR LOW RISK DEVICES 4 (2016), <https://perma.cc/Y2KF-X699> (PDF).

90. *See id.* at 3. Before the 21st Century Cures Act was enacted, it was the FDA’s policy not to enforce device requirements for many such products, meaning the law may not have changed the regulatory scheme in practice. *See, e.g.*, POLICY FOR DEVICE SOFTWARE FUNCTIONS AND MOBILE MEDICAL APPLICATIONS, *supra* note 87, at 12.

whole, but rather for the particular use that the manufacturer has proposed—to address a particular disease or condition, or have a particular effect on the body, for a specific population, and, for drugs, at a specified dose and in a specified dosage form.⁹¹ At the same time that the FDA authorizes a product—or more precisely, a particular use for the product—it also authorizes labeling that describes that use.⁹² Uses that the FDA has *not* authorized are *not* described in the FDA-authorized labeling, and thus are known as “off-label” uses.⁹³ In this way, the manufacturer’s intentions determine the focus of the FDA’s premarket authorization decision for a particular product, as well as the scope of the labeling that the FDA authorizes for the product.

This limited scope of FDA authorization, however, usually does not restrict how drugs and devices are actually used once they are marketed.⁹⁴ Consistent with the conventional view that states are the primary regulators of medical practice, it has long been the FDA’s position that health care providers generally may prescribe or administer a legally marketed drug or device for any use (and patients or consumers may use a legally marketed product for any purpose), including “off-label” uses.⁹⁵

91. See FDA MEMO, *supra* note 21, at 2–3; Nathan Cortez, *The Statutory Case Against Off-Label Promotion*, 83 U. CHI. L. REV. ONLINE 124, 126 (2016); Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1826 (1996).

92. See, e.g., Erika Lietzan, *The Drug Innovation Paradox*, 83 MO. L. REV. 39, 43 (2018); Sam F. Halabi, *The Drug Repurposing Ecosystem: Intellectual Property, Incentives, Market Exclusivity, and the Future of “New” Medicines*, 20 YALE J.L. & TECH. 1, 39 (2018).

93. See, e.g., Cortez, *supra* note 91, at 124.

94. See, e.g., Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the FDA, 37 Fed. Reg. 16,503, 16,503 (proposed Aug. 15, 1972) (to be codified at 21 C.F.R. pt. 130).

95. See, e.g., 21 U.S.C. § 396; FDA MEMO, *supra* note 21, at 3. There, however, are instances in which off-label use is prohibited or limited by FDA requirements (or state or Drug Enforcement Administration requirements). For example, the FDCA prohibits off-label prescribing of Human Growth Hormone (HGH). 21 U.S.C. § 333(e). The FDA also has the authority to require Risk Evaluation and Mitigation Strategies (REMS) for drugs and special controls and restrictions for devices, all of which can have the effect of limiting health care professionals’ ability to prescribe or dispense products off-label.

Indeed, off-label uses, including certain well-known non-therapeutic uses, are common.⁹⁶ For example, student use of Adderall (amphetamine aspartate), Ritalin (methylphenidate hydrochloride), and Provigil (modafinil) to improve academic performance has long been a high-profile, and controversial, example of performance-enhancing drug use.⁹⁷ All of these drugs, however, are approved for other, therapeutic uses—Adderall for ADHD and narcolepsy,⁹⁸ Ritalin for ADHD,⁹⁹ and Provigil for narcolepsy and other sleep disorders.¹⁰⁰ The FDA, therefore, has not evaluated the well-known performance-enhancing uses of these drugs.

At the same time that off-label uses are generally permitted, the FDA has long interpreted the FDCA as prohibiting manufacturers from promoting their drugs and

See, e.g., id. § 355-1; Patricia J. Zettler, *The Indirect Consequences of Expanded Off-Label Promotion*, 78 OHIO ST. L.J. 1053, 1081 (2017) [hereinafter *Indirect Consequences*].

96. *See* Tewodros Eguale et al., *Drug, Patient, and Physician Characteristics Associated with Off-Label Prescribing in Primary Care*, 172 ARCHIVES INTERNAL MED. 781, 781 (2012); Tewodros Eguale et al., *Association of Off-Label Drug Use and Adverse Drug Events in an Adult Population*, 176 J. AM. MED. ASS'N INTERNAL MED. 55, 60 (2016).

97. *See* Greely et al., *supra* note 33, at 702; *see also* GRAY MATTERS, *supra* note 36, at 37 (“[O]ne review of Provigil® and Ritalin® use for cognitive enhancement states that expectations regarding the effectiveness of these drugs exceed their actual effects.” (citations omitted)).

98. U.S. FOOD & DRUG ADMIN., ADDERALL LABELING, <https://perma.cc/KB4U-ZF5B> (PDF) (last updated Jan. 2017).

99. U.S. FOOD & DRUG ADMIN., RITALIN LABELING (Jan. 2017), <https://perma.cc/CLQ2-XTC9> (PDF).

100. U.S. FOOD & DRUG ADMIN., PROVIGIL LABELING, <https://perma.cc/3Z9X-HHFB> (PDF) (last updated Jan. 2015). One of Provigil’s approved indications is for excessive sleepiness associated with “shift work disorder.” *Id.* at 1. Characterizing the negative circadian rhythm effects of shift work as a disorder is an example of what some commentators have criticized as the medicalization of the problems of ordinary life (or the medicalization of a problem that may be best fixed through non-medical means, such as more humane workplace policies). *See, e.g.,* Robert Meadows et al., *The Sociology of Sleep*, in SLEEP, HEALTH, AND SOCIETY: FROM AETIOLOGY TO PUBLIC HEALTH 275, 277 (Francesco P. Cappuccio et al. eds., 2010).

devices for off-label uses.¹⁰¹ The FDA's policies on off-label promotion are controversial and have been subject to legal challenges grounded in the First Amendment.¹⁰² But the agency has yet to significantly change its approach to off-label promotion (and First Amendment challenges have yet to require the agency to do so).¹⁰³ Accordingly, although off-label uses are often not regulated by the FDA, manufacturers that wish to promote non-therapeutic uses of their drugs and devices generally must first obtain FDA authorization for those uses.

101. See, e.g., Cortez, *supra* note 91, at 130; FDA MEMO, *supra* note 21, at 29. The FDCA does not expressly prohibit the promotion of unauthorized uses. Instead, the FDCA prohibits distributing in interstate commerce misbranded, adulterated, or unauthorized new drugs and devices. 21 U.S.C. § 331(a). And, under the FDA's interpretation of the FDCA, when a manufacturer promotes an FDA-authorized drug or device for an unauthorized use, that causes a drug to be misbranded (or, in some cases, to be an unapproved new drug), and a device to be misbranded or adulterated. See, e.g., Cortez, *supra* note 91, at 130.

102. For a small selection of articles on off-label promotion, see Joshua M. Sharfstein & Alta Charo, *The Promotion of Medical Products in the 21st Century: Off-Label Marketing and First Amendment Concerns*, 314 J. AM. MED. ASS'N 1795, 1796 (2015); Ralph F. Hall & Elizabeth S. Sobotka, *Inconsistent Government Policies: Why FDA Off-Label Regulation Cannot Survive First Amendment Review Under Greater New Orleans*, 62 FOOD & DRUG L.J. 1, 1 (2007); George Horvath, *Off-Label Drug Risks: Toward A New FDA Regulatory Approach*, 29 ANNALS HEALTH L. & LIFE SCI. 101, 101 (2020); Jeffrey Chasnow & Geoffrey Levitt, *Off-Label Communications: The Prodigal Returns*, 73 FOOD & DRUG L.J. 257, 257 (2018); Joan H. Krause, *Truth, Falsity, and Fraud: Off-Label Drug Settlements and the Future of the Civil False Claims Act*, 71 FOOD & DRUG L.J. 401, 404 (2016); Aaron S. Kesselheim & Michelle M. Mello, *Prospects for Regulation of Off-Label Drug Promotion in an Era of Expanding Commercial Speech Protection*, 92 N.C. L. REV. 1539, 1542 (2014); David Orentlicher, *Off-Label Drug Marketing, the First Amendment, and Federalism*, 50 WASH. U. J.L. & POL'Y 89, 92 (2016); Christopher Robertson, *The Tip of the Iceberg: A First Amendment Right to Promote Drugs Off-Label*, 78 OHIO ST. L.J. 1019, 1020 (2017); John Kamp et al., *FDA Marketing v. First Amendment: Washington Legal Foundation Legal Challenges to Off-Label Policies May Force Unprecedented Changes at FDA*, 54 FOOD & DRUG L.J. 555, 555 (1999); *Indirect Consequences*, *supra* note 95, at 1061.

103. See FDA MEMO, *supra* note 21, at 20.

D. “Medical” Use

Caselaw and the FDA’s regulatory history also provide some possible limits on the drug and device definitions. In the 1960s and 1970s two circuit courts and one district court concluded that structure/function claims must be “medical” in nature to make a product—in those cases, a wrinkle cream—a drug or device.¹⁰⁴ Relying on these cases, the FDA also has stated in a few instances that a product must have a “medical application” to fall within the device definition, specifically.¹⁰⁵ For example, the agency declined to categorize as devices exercise equipment intended for recreational purposes as well as implantable chips used for non-medical identification purposes, despite the fact such products are clearly intended to affect the structure or function of the body.¹⁰⁶

Although requiring that drugs and devices have a “medical” application might, on its face, seem to exclude non-therapeutic uses from the FDA’s drug and device authorities, courts and the

104. See *United States v. An Article . . . Consisting of 216 Cartoned Bottles, More or Less, Sudden Change*, 409 F.2d 734, 742 (2d Cir. 1969); *United States v. An Article Consisting of 36 Boxes, More or Less, Labeled “Line Away Temp. Wrinkle Smoother, Coty,”* 415 F.2d 369, 372 (3d Cir. 1969); *United States v. Article of Drug 47 Ship. Cartons, More or Less, “Helene Curtis Magic Secret,”* 331 F. Supp. 912, 917 (D. Md. 1971); see also Anna Wexler, *A Pragmatic Analysis of the Regulation of Consumer Transcranial Direct Current Stimulation (tDCS) Devices in the United States*, 2 J.L. & BIOSCIENCES 669, 681 (2015) (discussing these cases).

105. See HUTT ET AL., *supra* note 56, at 125–28 (reprinting a 2002 letter from the FDA’s then-Chief Counsel stating that a microminiature transponder implant was not a device because it did not affect the body in a medical or drug-type fashion); *United States v. Undetermined No. of Unlabeled Cases*, 21 F.3d 1026, 1030 (10th Cir. 1994) (Cook, J., dissenting) (“The government concedes that it does not claim that a device which has no medical application could qualify as a device under the FDCA.” (citations omitted)); cf. Gary E. Gamberman, Note, *Intended Use and Medical Devices: Distinguishing Nonmedical “Devices” from Medical “Devices” Under 21 U.S.C. 321(h)*, 61 GEO. WASH. L. REV. 806, 807 (1993) (“[W]hen the manufacturer implies that the product has medicinal properties, courts have upheld FDA jurisdiction. Conversely, absent such representations, FDA assertion of jurisdiction has failed.”).

106. See *Physical Medicine Devices; General Provisions and Classification of 82 Devices*, 48 Fed. Reg. 53,032, 53,043 (Nov. 23, 1983) (to be codified at 21 C.F.R. pt. 890); HUTT ET AL., *supra* note 56, at 125–28.

agency have not consistently interpreted the drug and device definitions so narrowly. The courts that suggested that structure/function claims must have a “medical” connotation also construed a wide variety of claims, including claims such as “tighten[s] the skin,” to meet that standard—so long as the claims were “drug-type.”¹⁰⁷ In other cases, courts simply have not declared that structure/function claims must have a medical connotation to make a product a drug or device.¹⁰⁸ Likewise, notwithstanding its statements in the context of exercise equipment and implantable chips, the FDA has in some instances construed non-therapeutic uses of products to be drugs or devices—such as injectable dermal fillers intended to eliminate wrinkles or enhance lips, “micro-needling” machines intended to improve the skin’s texture or tone, and products intended for spider vein removal.¹⁰⁹ Indeed, if it were true that

107. See *Line Away*, 415 F.2d at 372; *Sudden Change*, 409 F.2d at 742. But see *Helene Curtis Magic Secret*, 331 F. Supp. at 915 (concluding that a wrinkle cream that made claims similar to those described in *Line Away* was not a drug).

108. See, e.g., *United States v. Storage Spaces Designated Nos. 8 & 49*, 777 F.2d 1363, 1366 (9th Cir. 1985) (stating that a product intended for use as a cocaine substitute was a drug under the FDCA); *Nutrilab, Inc. v. Schweiker*, 713 F.2d 335, 339 (7th Cir. 1983) (concluding that starch blockers are drugs because “they are intended to affect digestion in the people who take them”); *United States v. Travia*, 180 F. Supp. 2d 115, 119 (D.D.C. 2001) (concluding that nitrous oxide sold outside a rock concert was a drug); U.S. FOOD & DRUG ADMIN., Warning Letter to Arco Globus Trading LCC (Dec. 11, 2017), <https://perma.cc/W248-98NF> (concluding that products marketed as producing “euphoria” are drugs); U.S. FOOD & DRUG ADMIN., Warning Letter to ALV Supplement Direct, (Mar. 3, 2016), <https://perma.cc/E55L-6C2X> (concluding that products marketed as “boosting energy,” burning fat, and “increase[ing] focus” are drugs); cf. *Undetermined No. of Unlabeled Cases*, 21 F.3d at 1028 (“The [device] definition does not define the term ‘diagnosis’ nor limit diagnostic devices to those used prior to medical treatment.” (quoting 21 U.S.C. § 321(h)(2))).

109. See, e.g., *Warning Letters Highlight Differences Between Cosmetics and Medical Devices*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/V44AC-D4RH> (last updated Sept. 11, 2020) (listing examples of products for aesthetic uses that the FDA regulates as devices). The FDA’s seemingly contradictory positions may result from the agency broadly construing the term “medical.” For example, in 1993, the agency explained that it considered drugs intended to stop the habit of nailbiting to be intended to prevent disease, because nailbiting can make infection more likely. See *Nailbiting and Thumbsucking*

products must have medical uses—narrowly construed—to meet the definition of a device, it may not have been necessary for Congress to remove software intended for general wellness uses from the definition of a device, for example.¹¹⁰ In short, the courts’ and the FDA’s occasional reliance on “medical” use as a limit on the drug and device definitions is not entirely convincing, nor has it yielded a definitive, principled answer as to which non-therapeutic uses fall within the drug and device definitions, and which do not.¹¹¹

Deterrent Drug Products for Over-the-Counter Human Use, 58 Fed. Reg. 46,749, 46,750 (Sept. 2, 1993) (to be codified at 21 C.F.R. pt. 310.536). It also may be that the FDA did not accurately describe its overall policy in the documents in which it claimed specific products without medical applications were not devices.

110. See 21st Century Cures Act, Pub. L. No. 114-255, § 3060, 130 Stat. 1033, 1130 (2016).

111. The FDA’s ability to successfully assert jurisdiction over non-therapeutic uses might not be particularly dependent on formal doctrines of judicial deference to agencies’ interpretations of their enabling statutes and implementing regulations. *Cf.* Cary Coglianese, *Chevron’s Interstitial Steps*, 85 GEO. WASH. L. REV. 1339, 1344 (2017) (describing *Chevron* and “the emerging criticism of its deference principle”); Christopher J. Walker, *Attacking Auer and Chevron Deference: A Literature Review*, 16 GEO. J.L. & PUB. POL’Y 103, 105–18 (2018) (describing the arguments in favor of eliminating or narrowing *Chevron* and *Auer* deference). For the FDA specifically, courts have long deferred to the agency’s interpretations of the FDCA. *See, e.g.*, *United States v. An Article of Drug . . . Bacto-Unidisk . . .*, 394 U.S. 784, 791–92 (1969); *United States v. Rutherford*, 442 U.S. 544, 553 (1979); *Premo Pharm. Lab’ys, Inc. v. United States*, 629 F.2d 795, 803 (2d Cir. 1980); *cf.* Kent Barnett & Christopher J. Walker, *Chevron in the Circuit Courts*, 116 MICH. L. REV. 1, 53 (2017) (reporting that the FDA was among the agencies to which courts most often deferred); William N. Eskridge, Jr. & Lauren E. Baer, *The Continuum of Deference: Supreme Court Treatment of Agency Statutory Interpretations from Chevron to Hamdan*, 96 GEO. L.J. 1083, 1120 (2008) (“[T]he Court was highly deferential to agency interpretations before *Chevron*.”); Peter M. Shane, *Chevron Deference, the Rule of Law, and Presidential Influence in the Administrative State*, 83 FORDHAM L. REV. 679, 684 (2014) (“[C]ommentators were hardly unanimous in . . . characteriz[ing] . . . *Chevron* as ‘revolutionary.’”); David Zaring, *Reasonable Agencies*, 96 VA. L. REV. 135, 143 (2010) (“[C]ourts tend to reverse agencies at the same rate regardless of the standard of review they apply . . .”). *But see* *Genus Med. Techs., LLC v. United States Food & Drug Admin.*, 427 F. Supp. 3d 74, 84 (D.D.C. 2019) (declining to defer to the FDA’s position that the drug and device definitions are overlapping). Perhaps more importantly given the current composition of the Supreme Court, regardless

E. *Other Statutory Schemes*

Another ground that courts, and arguably the FDA, have used to limit the scope of the FDA's drug and device jurisdiction is that certain non-therapeutic uses are regulated pursuant to later-enacted federal statutes other than, and more specific than, the FDCA—and thus Congress could not have intended the FDA to regulate them.¹¹² One example comes from the majority opinion in *FDA v. Brown & Williamson Tobacco Corp.*¹¹³ In 1996, before Congress expressly granted FDA jurisdiction over tobacco products, the FDA promulgated a rule that asserted that nicotine was a drug, intended to affect the structure or function of the body, and that the agency had authority to regulate cigarettes and smokeless tobacco products as drug-delivery devices.¹¹⁴ Four years later, in *Brown & Williamson*, the Supreme Court invalidated the rule on statutory interpretation grounds.¹¹⁵ Specifically, a five-judge majority concluded that tobacco products were not drugs or

of judicial deference to an agency position, the plain text of the drug and device definitions lend themselves to an expansive interpretation. Cf. Charlton C. Copeland, *Another Explanation of Justice Gorsuch's Bostock Vote*, REGUL. REV. (July 22, 2020), <https://perma.cc/J2MZ-ZUND> (observing that Justice Gorsuch's strict textualism produced an expansive interpretation of Title VII protections, contradicting expectations based on political alignment); see also *Bostock v. Clayton County.*, 140 S. Ct. 1731, 1737 (2020) ("When the express terms of a statute give us one answer and extratextual considerations suggest another, it's no contest. Only the written word is the law, and all persons are entitled to its benefit.").

112. See, e.g., *Food & Drug Admin. v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000).

113. *Id.*

114. See generally DAVID KESSLER, *A QUESTION OF INTENT: A GREAT AMERICAN BATTLE WITH A DEADLY INDUSTRY* (2001). A drug-delivery device is a kind of combination product. Combination products are products "comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity." 21 C.F.R. § 3.2(e)(1) (2020). The FDA regulates combination products consistent with its "primary mode of action," which is mode of action that is expected to give the greatest contribution to the product's effects. 21 U.S.C. § 353(g)(1).

115. *Brown & Williamson Tobacco Corp.*, 529 U.S. at 133.

devices under the FDCA. One reason, among others, that the majority offered was that “Congress ha[d] enacted six separate pieces of legislation . . . addressing the problem of tobacco use and human health,” none of which provided the FDA a role in regulating tobacco products.¹¹⁶

The intersection of the FDA’s jurisdiction with that of the Consumer Products Safety Commission (CPSC) offers additional examples. For instance, the CPSC’s statutory authority over consumer products was one reason the FDA cited in 2002 for declining to assert jurisdiction over an implantable chip used for non-medical identification purposes.¹¹⁷ As a second example, in 2003 the Second Circuit struck down an FDA regulation requiring certain child-proof packaging for drugs and dietary supplements partly because the Poison Prevention Packaging Act “specifically and unambiguously targets the accidental poisoning problem” and it is the CPSC—not the FDA—that administers that law.¹¹⁸

This limit on the FDA’s jurisdiction, however, is unlikely to clearly exclude all, or perhaps even many, emerging non-therapeutic uses.¹¹⁹ Congress has not enacted laws (other than the FDCA) that specifically regulate many non-therapeutic uses, such as cognitive enhancement technologies, akin to how the *Brown & Williamson* majority described the non-FDCA laws that specifically targeted tobacco products.¹²⁰ Drugs intended for recreational uses are one obvious exception. Congress has enacted non-FDCA legislation that specifically addresses many of these products, through, for example, the federal Controlled Substances Act (CSA). But the CSA expressly envisions the

116. *Id.* at 143.

117. HUTT ET AL., *supra* note 56, at 125–28.

118. *Nutritional Health All. v. Food & Drug Admin.*, 318 F.3d 92, 104 (2d Cir. 2003).

119. *Cf.* Noah, *supra* note 14, at 4 (asserting that the FDA possibly could assert jurisdiction over firearms notwithstanding the many non-FDCA federal laws specifically governing firearms).

120. *Cf. Brown & Williamson Tobacco Corp.*, 529 U.S. at 133 (describing “the tobacco-specific legislation that Congress has enacted”).

FDA playing a role in regulating controlled substances.¹²¹ Even after the enactment of the CSA, the federal government has continued to assert that certain substances intended for recreational uses are drugs under the FDCA.¹²² Moreover, to the extent that Congress is considering reforming the CSA through descheduling certain substances intended for recreational uses, it has thus far not seemed to consider exempting such substances from the FDCA's drug definition.¹²³ Thus, even for drugs intended for recreational uses that are subject to other federal laws, courts may not determine that the FDA lacks jurisdiction.

F. *Safety and Effectiveness*

Yet another, potentially powerful, line of reasoning that has been offered to limit the scope of the drug and device definitions is the argument that it would be impossible for the FDA to determine that non-therapeutic uses of drugs and devices are safe and effective. Under this view, the FDCA's standard for demonstrating safety and effectiveness would create an effective ban on non-therapeutic uses.¹²⁴ Thus, if Congress did not intend to ban such technologies, it could not have intended them to be drugs and devices subject to FDA jurisdiction.

This argument has been used to limit the scope of FDA jurisdiction in two high-profile—and arguably, highly politicized—instances. The first again involves the FDA's attempt to assert jurisdiction over tobacco products in 1996 and

121. See, e.g., Patricia J. Zettler et al., *Implementing A Public Health Perspective in FDA Drug Regulation*, 73 FOOD & DRUG L.J. 221, 240 (2018).

122. See, e.g., *United States v. Travia*, 180 F. Supp. 2d 115, 119 (D.D.C. 2001); cf. *Graves v. New York ex rel. O'Keefe*, 306 U.S. 466, 479 (1939) (discussing the idea of congressional acquiescence, where the silence of Congress, particularly when it has opportunities to amend a statute, may indicate its agreement with a particular statutory interpretation).

123. See, e.g., *Marijuana Opportunity Reinvestment and Expungement Act of 2020*, H.R. 3884, 116th Cong. (2020), <https://perma.cc/RD75-UXAS>; cf. O'Connor & Lietzan, *supra* note 66 (discussing the FDA's extensive jurisdiction over cannabis intended for medical uses, even after descheduling).

124. See, e.g., *Food & Drug Admin. v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 137 (2000).

FDA v. Brown & Williamson Tobacco Corp. In addition to citing the federal laws specifically regulating tobacco products to support its conclusion that FDA lacked jurisdiction, the majority in *Brown & Williamson* also reasoned that the FDA could not determine tobacco products to be safe and effective, and, therefore, FDA oversight would amount to a ban on the products.¹²⁵ Because the majority determined that Congress did not intend to ban tobacco products altogether, the majority reasoned that Congress could not have intended the FDA to regulate tobacco products.¹²⁶ Notably, the majority reached this conclusion without disagreeing that tobacco products are intended to affect the structure or function of the body—and despite the fact that the FDA itself said that it could find certain tobacco products to be safe and effective.¹²⁷

The argument that the FDA could not find tobacco products to be safe and effective might be persuasive, given the well-known harms associated with the products. But this reasoning has been extended elsewhere more recently. As states increasingly have turned to purchasing substances for lethal injection executions that the FDA has not approved,¹²⁸ states have faced legal challenges grounded in arguments that they are obtaining drugs in violation of the FDCA.¹²⁹ Against this

125. *Id.* The majority offered several additional reasons, including that Congress had enacted more specific statutes to regulate tobacco products as noted in Part II.E.

126. *Id.*

127. *Id.* at 139. The FDA argued, for example, that tobacco products could be viewed as safe and effective because a ban on the addictive products would have negative public health effects. *See Regulations Restricting the Sale and Distribution of Cigarettes and Smokeless Tobacco to Protect Children and Adolescents*, 61 Fed. Reg. 44,396, 44,397 (Aug. 28, 1996) (to be codified at 21 C.F.R. pts. 801, 803, 804, 807, 820, 897).

128. *See, e.g.,* Seema K. Shah, *Experimental Execution*, 90 WASH. L. REV. 147, 173 (2015).

129. *See, e.g.,* *Cook v. FDA*, 733 F.3d 1, 3 (D.C. Cir. 2013). States have turned to illicit supply chains for various reasons, including that legitimate pharmaceutical companies have stopped manufacturing the substances used for executions or have stopped being willing to sell substances for executions, particularly since the European Union's 2011 prohibition on trade in "goods which could be used for capital punishment." Commission Implementing Regulation 1352/2011, 2011 O.J. (L 338) 31.

background, in May 2019 the Department of Justice's Office of Legal Counsel (OLC) issued an opinion—that is binding on FDA—asserting that substances intended for human executions are not “drugs” within FDA's authority.¹³⁰ Among other reasons, the OLC explained that such substances cannot be drugs because “the regulation of such articles under the FDCA would effectively require their prohibition because they could hardly be found ‘safe and effective’ for such an intended use.”¹³¹ Similar to the majority opinion in *Brown & Williamson*, OLC reached this conclusion even though it acknowledged that “[a]rticles used in capital punishment do literally ‘affect the structure or any function of the body.’”¹³² Moreover, as OLC also acknowledged, the FDA had long regulated substances for animal euthanasia as drugs,¹³³ concluding that they are safe and effective for that purpose when they “result[] in a humane and painless death.”¹³⁴

Although this argument regarding safety and effectiveness has, so far, been employed in these somewhat limited circumstances—for tobacco products and for means of execution—it is not difficult to imagine its application to emerging markets of non-therapeutic uses that otherwise could fall within the drug and device definitions.¹³⁵ For example, as state and local governments decriminalize recreational cannabis (and other botanical drugs, such as psychedelic mushrooms), arguments that, notwithstanding their effect on the body's function, the FDA should not regulate recreational uses of drugs because it cannot assess the safety and

130. See 2019 OLC Memo, *supra* note 17, at 1.

131. *Id.* (citing *Brown & Williamson*, 529 U.S. at 137–39).

132. *Id.* at 10 (citing 21 U.S.C. § 321(g)(1)(C), (h)(3)).

133. See *id.* at 15 n.9.

134. *Compliance Policy Guide § 650.100 Animal Drugs for Euthanasia*, U.S. FOOD & DRUG ADMIN. (Mar. 1995), <https://perma.cc/3PQQ-JWTX>.

135. Cf. Noah, *supra* note 14, at 37 (considering pathways to marketing a ‘safe and effective’ firearm, if the FDA asserted jurisdiction over firearms as devices).

effectiveness are likely to emerge.¹³⁶ As another example, companies are increasingly showing interest in developing brain stimulation machines or brain-computer interfaces to enhance cognitive function rather than to treat disorders like depression, and commentators have begun to raise questions about whether FDA could consider such technologies to be safe and effective.¹³⁷ Accordingly, assessing the validity of safety and effectiveness as a limit on the drug and device definitions is useful for understanding the regulatory landscape for new markets and technologies.

III. EVALUATING THE SAFETY AND EFFECTIVENESS OF NON-THERAPEUTIC USES

This Part argues for skepticism about limiting the FDA's jurisdiction based on arguments that the FDA could never determine that non-therapeutic uses are safe and effective. As a descriptive matter, such arguments will rarely be correct. The FDA assesses drug and device uses on a case-by-case basis, and the FDCA and FDA regulations give the agency tremendous flexibility in determining what evidence is needed to demonstrate that the benefits of a particular use outweigh its risks.¹³⁸ Moreover, a careful review demonstrates that the agency has a not-insubstantial track record of evaluating the safety and effectiveness of non-therapeutic uses and has not judged those non-therapeutic uses to be without significant benefits.¹³⁹ This is not to say that the agency treats therapeutic

136. Cf. Benton Bodamer (@TripleB_Esq), TWITTER (Jan. 30, 2020 10:14 PM), <https://perma.cc/5EFJ-2R9U> (showing a tweet from an attorney with expertise in cannabis raising a similar concern about psychedelic mushrooms).

137. See, e.g., Nick Statt, *Elon Musk Launches Neuralink, a Venture to Merge the Human Brain with AI*, VERGE (Mar. 27, 2017, 4:10 PM), <https://perma.cc/FGJ5-PJML>; Lucille M. Tournas & Walter G. Johnson, *Elon Musk Wants to Hack Your Brain*, SLATE (Aug. 5, 2019, 7:30 AM), <https://perma.cc/MXH9-8JSK>.

138. See Merrill, *supra* note 91, at 1782 (“FDA exercises effectively unchallengeable authority to dictate the number and kinds of studies required to support approval and nearly unreviewable discretion to interpret the results.”).

139. See *infra* Part III.B.

and non-therapeutic uses identically—there are instances, such as with silicone breast implants, when the agency was willing to authorize therapeutic uses when it did not authorize non-therapeutic ones.¹⁴⁰ But, for non-therapeutic uses, the agency is more tolerant of serious risks, including risks of death, and relatively lower benefits than might be expected.¹⁴¹

A. *Flexible Statutory Standards*

The FDA's role in approving drugs and devices is, perhaps, the most well-known way that it evaluates products' safety and effectiveness. For drugs, this approval authority applies to “new drugs”¹⁴² that are not “generally recognized . . . as safe and effective,”¹⁴³ including in the FDA's view most, if not all, prescription drugs as well as certain over-the-counter (OTC) drugs.¹⁴⁴ Devices undergo more varied forms of premarket review than drugs do, with the type of review typically depending on the level of risk posed by a device and its novelty.¹⁴⁵ The highest risk, “class III” devices—such as

140. See Mehlman, *supra* note 24, at 702.

141. Cf. *id.* at 699–703 (“[E]ither . . . the [FDA] feels that the risks posed by saline implants are so small that they are outweighed by cosmetic as well as by therapeutic benefits, or . . . the agency simply has not come to grips with the enhancement/therapy distinction.”).

142. 21 U.S.C. § 355(a).

143. *Id.* § 321(p).

144. General recognition of safety and effectiveness is a high bar to clear that requires at least as much evidence of safety and effectiveness as FDA approval does. See, e.g., *Weinberger v. Hynson, Wescott & Dunning, Inc.*, 412 U.S. 609, 629 (1973). In addition, to fall outside of the definition of a “new drug” a drug must have been marketed to a material extent and for a material time—which the FDA generally interprets as requiring that the drug has been legally marketed in sufficient quantities, for example in another country, for at least five years. See 21 U.S.C. 321(p)(2); U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: TIME AND EXTENT APPLICATIONS FOR NONPRESCRIPTION DRUG PRODUCTS 6 (2011), <https://perma.cc/45SZ-S8S2> (PDF).

145. See Merrill, *supra* note 91, at 1109–11 (describing the different forms of premarket review that apply to different device classifications based on risk profile); W. Nicholson Price, II, *Regulating Black-Box Medicine*, 116 MICH. L. REV. 421, 438 (2017) (same).

pacemakers and implanted brain stimulators—typically require FDA approval.¹⁴⁶

The precise language of the statutory standards for approving new drugs under a new drug application (NDA) and devices under a premarket approval application (PMA) differ.¹⁴⁷ But the general idea is the same: to approve a use of new drug or device, the FDA must determine that the product is safe and effective for its proposed indication and that the proposed labeling is not false or misleading.¹⁴⁸ Because drugs and devices

146. See 21 U.S.C. § 360c(a)(1)(C).

147. Compare *id.* § 355(d) (describing grounds for refusing to approve a new drug application), with *id.* § 360e(d)(2) (describing grounds for refusing premarket approval of a device). Specifically, the drug approval standard requires, among other things, “adequate tests” to show the drug is safe and “substantial evidence” of effectiveness, demonstrated through “adequate and well-controlled investigations.” *Id.* § 355(d). The device approval standard requires “reasonable assurance” of safety and effectiveness consisting of “one or more” “well-controlled investigations” or other “valid scientific evidence.” *Id.* §§ 360c(a)(3), 360e(d). Whether these standards are the same—or instead, the device standard is a lower one—in practice and as a statutory interpretation matter, is debated. See Peter Barton Hutt et al., *The Standard of Evidence Required for Premarket Approval Under the Medical Device Amendments of 1976*, 47 FOOD & DRUG L.J. 605, 608–09 (1992) (“Congress intended medical device manufacturers seeking premarket approval to be subject to a different, more flexible, standard of evidence of safety and effectiveness than new drug sponsors.”); Merrill, *supra* note 91, at 1821–23 (arguing that Congress did not intend the device model to mimic the drug model but acknowledging the FDA’s post-1993 policy shift toward equally rigorous expectations for approval of both drugs and devices).

148. See 21 U.S.C. § 355(d). This Article focuses on drugs approved under “new drug applications” (NDAs) pursuant to 21 U.S.C. § 355(b)(1), which are often thought of as “brand-name” drugs. The FDA also approves generic new drugs through a separate, abbreviated process. See *id.* § 355(j). As with other FDA authorization processes, FDA review and approval of abbreviated new drug applications (ANDAs) is intended to assure the safety and effectiveness of the drugs. See *id.* § 355(j). This goal, however, is accomplished by demonstrating that the generic drug is the same as the brand-name drug (with a few minor exceptions not related to safety and effectiveness). From that similarity, the safety and effectiveness of the generic drug can be inferred. See *id.* Thus, by the time the FDA would evaluate an ANDA for a non-therapeutic use, the agency would have already made the determination most relevant to this Article—the initial determination that the non-therapeutic use is safe and effective when it approved the brand-name drug for that use. Cf. Eric Biber & J.B. Ruhl, *The Permit Power Revisited: The Theory and Practice of Regulatory*

cannot be completely risk-free (and are not equally effective for all people), “safe and effective” generally means that the benefits of the product’s intended use outweigh its risks.¹⁴⁹ The FDCA requires that the drug or device manufacturer submit to the FDA numerous kinds of information showing that this approval standard is met, which typically consists of data from one or two well-designed clinical trials.¹⁵⁰ Once a use of a drug or device is approved the FDA’s weighing of its risks and benefits does not end. The FDA also regulates marketed products, including having the authority to withdraw an approval if the agency determines that the benefits of the product’s uses no longer outweigh its risks—perhaps because new risk information comes to light, as can happen once a product is used widely and outside of a controlled research environment.¹⁵¹

Although this overview makes safety and effectiveness determinations sound straightforward, there is inevitably uncertainty in scientific evidence and making benefit-risk determinations inherently involves certain value judgments.¹⁵² Perhaps for this reason, the FDCA, at least arguably, gives the FDA substantial discretion to decide what evidence is sufficient

Permits in the Administrative State, 64 DUKE L.J. 133, 190 (2014) (describing the ANDA process as an example of the government’s permitting power).

149. See generally Erika Lietzan & Patricia J. Zettler, *Regulating Medicines in the United States*, in OXFORD HANDBOOK ON COMPARATIVE HEALTH LAW (David Orentlicher & Tamara Hervey eds., Oxford Univ. Press 2020).

150. 21 U.S.C. § 355(d).

151. See *id.* § 355(e) (describing the bases upon which the Secretary may withdraw approval of a new drug application in light of information discovered later); *id.* § 360e(e) (same with respect to devices); 21 C.F.R. § 814.46 (2020) (allowing for withdrawal of premarket approval for devices pursuant to 21 U.S.C. § 360e(e)).

152. See Efthimios Parasidis et al., *Assessing COVID-19 Emergency Use Authorizations*, FOOD & DRUG L.J. (forthcoming 2021) (manuscript at 163) (on file with author) (making a similar point); cf. Eli Y. Adashi et al., *When Science and Politics Collide: Enhancing the FDA*, 364 SCI. 628, 630 (2019) (“Determining the basic facts about safety, efficacy, or adverse events reporting should be science-driven and as apolitical as possible.”); Craig J. Konnoth, *Drugs’ Other Side Effects*, 105 IOWA L. REV. 171, 206–07 (2019) (noting that FDA is a “political entity”).

to show that the benefits of a particular use of a drug or device outweigh its risks.¹⁵³ For example, in its regulations regarding new drug approvals, the FDA states that it must “exercise its scientific judgment to determine the kind and quantity of data and information an applicant is required to provide for a particular drug to meet the statutory standards [for safety and effectiveness].”¹⁵⁴

Consistent with the wide discretion granted to the FDA in the statute and implementing regulations, the FDA has determined that varying kinds of evidence are sufficient (or not) to demonstrate safety and effectiveness of different uses of drugs and devices, and varying kinds of risks and benefits produce favorable (or not) benefit-risk ratios.¹⁵⁵ One controversial example was the FDA’s 2016 decision to approve Exondys 51 (eteplirsen) for Duchenne muscular dystrophy, a severe form of the disease that almost exclusively affects boys and is associated with life expectancies only into patients’ twenties.¹⁵⁶ The FDA approved Exondys 51 based on an uncontrolled trial in just twelve patients, and against the recommendation of the agency’s Peripheral and Central Nervous System Drugs Advisory Committee.¹⁵⁷ This decision

153. Merrill, *supra* note 91, at 1782; cf. Konnoth, *supra* note 152, at 173–74 (arguing that FDA should take a broad approach to the evidence relevant to its approval decision).

154. 21 C.F.R. § 314.105(c) (2020).

155. See, e.g., U.S. FOOD & DRUG ADMIN., FACTORS TO CONSIDER WHEN MAKING BENEFIT-RISK DETERMINATIONS IN MEDICAL DEVICE PREMARKET APPROVAL AND DE NOVO CLASSIFICATIONS: GUIDANCE FOR INDUSTRY AND FOOD AND DRUG ADMINISTRATION STAFF, (2019), <https://perma.cc/N2A7-9JYL> (PDF); Wallach et al., *supra* note 18, at 220.

156. See *Duchenne and Becker Muscular Dystrophy*, MEDLINEPLUS, <https://perma.cc/C9P4-8V7P> (last updated Aug. 18, 2020).

157. See, e.g., Aaron S. Kesselheim & Jerry Avorn, *Approving a Problematic Muscular Dystrophy Drug: Implications for FDA Policy*, 316 JAMA 2357, 2357 (2016). It is worth noting that, in the wake of seemingly unprecedented political interference with FDA decision-making during the COVID-19 pandemic, see, for example, Parasidis et al., *supra* note 152, at 165, the process that the FDA followed in approving Exondys 51 has, in some ways, aged well. Specifically, the highest-ranking relevant career official determined the drug would be approved, over the objection of other career staff. The FDA Commissioner, a political appointee, let that decision stand partly because of

caused strong disagreement within the agency,¹⁵⁸ as well as vocal criticism from scholars.¹⁵⁹ Even among critics of the decision, however, few, if any, argued that the FDA failed to comply with the FDCA in determining that Exondys 51 met the safety and effectiveness standard for approval.

B. *Applying the Standards to Non-Therapeutic Uses*

The following four examples (two drug and two device)—although not exhaustive—demonstrate how the FDA has applied the flexible statutory standards for safety and effectiveness when approving non-therapeutic uses.¹⁶⁰ These

a strong norm within the agency that career staff, rather than political staff, typically make these decisions. See Memorandum from Robert M. Califf, Comm'r of Food & Drugs, to Janet Woodcock, Dir, CDER 2 (Sept. 16, 2016), available at <https://perma.cc/7A7M-XLHE> [hereinafter EXONDYS 51 MEMO].

158. See, e.g., EXONDYS 51 MEMO, *supra* note 157, at 17.

159. See, e.g., Kesselheim & Avorn, *supra* note 157, at 2357; see also Rebecca S. Eisenberg & Deborah B. Leiderman, *Cannabis for Medical Use: FDA and DEA Regulation in the Hall of Mirrors*, 74 FOOD & DRUG L.J. 246, 279 n.191 (2019) (describing the Exondys 51 approval as “controversial”); Jordan Paradise, *Three Framings of “Faster” at the FDA and the Federal Right to Try*, 11 WAKE FOREST J.L. & POL’Y 53, 81 (2020) (describing the “controversial” Exondys 51 approval and explaining that “[i]n a stunningly similar manner, the FDA recently approved . . . a second DMD drug from Sarepta [the Exondys 51 manufacturer], in December 2019”).

160. These examples focus on new drug applications and premarket approval applications, where the FDCA standards for safety and effectiveness are most relevant for this Article’s analysis. Most legally marketed devices, however, are not FDA-approved. See, e.g., U.S. GOV’T ACCOUNTABILITY OFF., GAO-09-190, MEDICAL DEVICES: FDA SHOULD TAKE STEPS TO ENSURE THAT HIGH-RISK DEVICE TYPES ARE APPROVED THROUGH THE MOST STRINGENT PREMARKET REVIEW PROCESS 6 (2009). Instead, manufacturers of low-risk devices generally do not have any premarket notification requirements, while manufacturers of moderate risk devices—class II devices, the class into which most devices fall—frequently obtain FDA “clearance” for marketing their devices by submitting an application known as a “510(k).” A 510(k) demonstrates that a manufacturer’s device is “substantially equivalent” to a device already on the market—it has the same intended use and the same technological characteristics as a “predicate device,” which allows the FDA to infer that the new device is as safe and effective as the currently marketed one. See, e.g., Ralph F. Hall & Michelle Mercer, *Rethinking Lohr: Does “SE” Mean Safe and Effective, Substantially Equivalent, or Both?*, 13 MINN. J.L. SCI. & TECH. 737, 753–54 (2012) (describing the process for showing substantial

examples suggest both that the agency has accepted varied evidence as showing safety and effectiveness of non-therapeutic uses, and that agency review is not an insurmountable obstacle to marketing non-therapeutic uses.

1. Hair Growth Drugs

Hair growth drugs—first approved roughly thirty years ago, when the FDA approved Rogaine¹⁶¹—provide examples of lucrative non-therapeutic uses, which the FDA approved based on relatively minimal evidence of effectiveness or despite relatively serious risks. When the FDA first approved Rogaine, its active ingredient, minoxidil, was already approved at the time—but for a therapeutic use (hypertension) and in a tablet, rather than topical form.¹⁶² It was through developing the therapeutic use of minoxidil, when subjects in clinical trials began to experience hair growth, that the manufacturer, The Upjohn Company (Upjohn), came to learn that the drug may have the potential to address hair loss as well.¹⁶³

equivalence). It is through 510(k) process, for example, that the FDA has authorized the marketing of certain decorative contact lenses. *See, e.g.*, DECORATIVE LENSES GUIDANCE, *supra* note 4, at 3.

161. *See* U.S. FOOD & DRUG ADMIN., *Rogaine Approval History*, <https://perma.cc/74U4-6VMQ> (detailing Rogaine's approval history). Although hair loss can be a result of medical problems or treatments, such as low thyroid conditions or chemotherapy drugs, and in such circumstances may be viewed as a medical problem, the drugs approved for regrowing hair do not improve or prevent such hair loss according to their FDA-approved labeling. *Cf.* EEOC v. United Parcel Serv., Inc., 141 F. Supp. 2d 1216, 1219 n.2 (D. Minn. 2001) (concluding that a health plan's decision to exclude Propecia was unlike its decision to exclude hormonal birth control pills because Propecia is a "non-medically necessary and elective treatment[]").

162. *See Loniten Approval History*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/RW6V-USX8>; *see also* W. Nicholson Price, II, *Making Do in Making Drugs: Innovation Policy and Pharmaceutical Manufacturing*, 55 B.C. L. REV. 491, 562 n.229 (2014) (discussing minoxidil's patent history). For a discussion of how new uses for already authorized products are developed, *see* Erika Lietzan, *Paper Promises for Drug Innovation*, 26 GEO. MASON L. REV. 168, 171–77 (2018).

163. *See, e.g.*, *Upjohn Co. v. Riahom Corp.*, 641 F. Supp. 1209, 1212 (D. Del. 1986).

Presumably because the tablet form of minoxidil was associated with serious cardiovascular adverse effects and a systemic effect of the drug was not needed for hair growth,¹⁶⁴ Upjohn sought to develop a topical version.¹⁶⁵ Upjohn spent three years conducting clinical trials, which ultimately showed that 26 percent of men using the topical formulation reported “moderate to dense hair regrowth” at four months, compared to 11 percent in the placebo groups.¹⁶⁶ In studies of women taking the drug, 19 percent reported moderate hair growth at 8 months, compared to 7 percent in the placebo group.¹⁶⁷

Although those numbers do not seem particularly impressive, the risks associated with the topical version of minoxidil—scalp irritation being the most common one—are not particularly serious.¹⁶⁸ And the FDA determined that the benefits of topical minoxidil outweighed its risks, ultimately approving it to regrow hair on the scalp in 1988 for men and in 1991 for women, as a prescription drug.¹⁶⁹ Likely partly because of its relatively minor risks, the FDA approved an application to switch Rogaine to over-the-counter status in 1996.¹⁷⁰

The FDA originally approved the other leading hair regrowth drug—a tablet called Propecia—in 1997.¹⁷¹ As with

164. See U.S. FOOD & DRUG ADMIN., LONITEN LABELING (2015), <https://perma.cc/A53S-2YRH> (PDF) (containing the FDA’s minoxidil labeling data).

165. See *Upjohn*, 641 F. Supp. at 1213.

166. See U.S. FOOD & DRUG ADMIN., ROGAINE LABELING (2005), <https://perma.cc/LP9V-747R> (PDF); see also *Upjohn*, 641 F. Supp. at 1213 (describing the time and money that Upjohn spent on developing Rogaine). Since the original formulation was approved, a stronger formulation has been approved for which studies have shown increased effectiveness. See U.S. FOOD & DRUG ADMIN., NDA 20-834 (1997), <https://perma.cc/PVX9-64BH> (PDF).

167. See ROGAINE LABELING, *supra* note 166.

168. See *id.*

169. See, e.g., Will Lester, *Hair-Raising Tale: No Fame for Men Who Discovered Rogaine*, DAILY GAZETTE (May 13, 1996), at A6.

170. See *Rogaine Approval History*, *supra* note 161. For a discussion of some of the business reasons that manufacturers may follow this pattern of first marketing a drug as a prescription-only, and later requesting a switch to OTC status, see Valerie Junod, *Drug Marketing Exclusivity Under United States and European Union Law*, 59 FOOD & DRUG L.J. 479, 514 (2004).

171. See *Propecia Approval History*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/3EGX-DUFY>.

Rogaine, the active ingredient in Propecia, finasteride, had been previously approved for a therapeutic use: for treating enlarged prostates causing urinary and other problems in men.¹⁷² The therapeutic version of finasteride, however, was approved at a dosage five times higher than was needed for the hair growth indication and Merck, the manufacturer, sought approval of a lower dose for hair growth in men.¹⁷³

Propecia's effectiveness was demonstrated in three randomized, controlled, blinded clinical trials of men with moderate to mild hair loss, looking at subjects' hair counts and self-assessments.¹⁷⁴ The trials showed that men using Propecia were rated as having significantly more hair on both measures than were the men using the placebo—for example, at twelve months, 65 percent of men using Propecia were rated as having increased growth compared to 37 percent of men in the placebo group.¹⁷⁵ Propecia is, however, associated with significant risks. At the time of its original approval, the drug was known to be associated with risks to male fetuses if taken by pregnant women and with effects on Prostate-Specific Antigen levels,

172. See *Proscar Approval History*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/9YU9-B3GN>; see also Lars Noah, *This Is Your Products Liability Restatement on Drugs*, 74 BROOK. L. REV. 839, 874–75 (2009) (“[O]ne decade later, the totality of published research continues to support the widespread use of this still-approved drug for treating [enlarged prostate].”). A third drug, dutasteride, was approved shortly after finasteride for a similar therapeutic purpose. See *Avodart Approval History*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/B38X-C8ZQ>. Although studies have suggested dutasteride may be effective for hair growth in men, it is not approved for that indication. See, e.g., Elise A. Olson et al., *The Importance of Dual 5 α -Reductase Inhibition in the Treatment of Male Pattern Hair Loss: Results of a Randomized Placebo-Controlled Study of Dutasteride Versus Finasteride*, 55 J. AM. ACAD. DERMATOLOGY 1014, 1022–23 (2006).

173. See Noah, *supra* note 172, at 875 (describing the history of Propecia's development and noting the risks associated with pill splitting). The higher dose of finasteride is associated with certain risks, such as an increased risk of breast cancer in men, that the lower dose is not known to be. See Steve T. Bird et al., *Male Breast Cancer and 5 α -Reductase Inhibitors Finasteride and Dutasteride*, 190 J. UROLOGY 1811, 1811 (2013).

174. See U.S. FOOD & DRUG ADMIN., PROPECIA LABELING (2014), <https://perma.cc/5543-YPPU> (PDF).

175. See *id.*

which are used to screen for prostate cancer.¹⁷⁶ In 2011, it became known that the drug is also associated with an increased risk of high-grade prostate cancer.¹⁷⁷ Despite these risks, the FDA approved, and has not withdrawn its approval of, finasteride for hair loss—instead choosing to mitigate the risks through approving the drug only for men, including warnings in the FDA-approved labeling, and continuing to require a prescription for the drug.¹⁷⁸

In addition to the differences in the formulations between the therapeutic and non-therapeutic versions of minoxidil (Rogaine's active ingredient) and finasteride (Propecia's active ingredient), the manufacturers likely sought approval of the hair loss indications—rather than simply relying on off-label use—because they wanted to actively promote those indications. Rogaine's initial approval in 1988 came shortly after the FDA's policies on direct-to-consumer (DTC) advertising of prescription drugs became more permissive.¹⁷⁹ Rogaine's manufacturer, Upjohn, then began one of the first DTC “disease awareness” advertising campaigns,¹⁸⁰ which featured individuals describing the “problems” associated with hair loss (e.g., “Can an emerging bald spot . . . damage your ability to get along with others,

176. See U.S. FOOD & DRUG ADMIN., NDA 20-834 APPROVAL PACKAGE (1997) <https://perma.cc/S85B-PVC8> (PDF).

177. See U.S. FOOD & DRUG ADMIN., PROPECIA (LABELING) (2011), <https://perma.cc/DJ4S-BQX3> (PDF). Concerns about other risks associated with the drug, such as erectile dysfunction and depression, have also been raised. See, e.g., Dan Levine, *Court Let Merck Hide Secrets about a Popular Drug's Risks*, REUTERS (Feb. 11, 2019), <https://perma.cc/59KG-357H>.

178. See *id.*

179. See Direct-to-Consumer Advertising of Prescription Drugs; Withdrawal of Moratorium (Notice), 50 Fed. Reg. 36,677, 36,678 (Sept. 9, 1985); see also Wayne L. Pines, *A History and Perspective on Direct-to-Consumer Promotion*, 54 FOOD & DRUG L.J. 489, 493 (1999) (describing how companies undertook more aggressive “help-seeking” advertisements after the FDA lifted restrictions in 1985).

180. See Jon D. Hanson & Douglas A. Kysar, *Taking Behavioralism Seriously: Some Evidence of Market Manipulation*, 112 HARV. L. REV. 1420, 1456 (1999); see also Lars Noah, *Advertising Prescription Drugs to Consumers: Assessing the Regulatory and Liability Issues*, 32 GA. L. REV. 141, 142 n.4 (1997) (elaborating on the pharmaceutical industry's efforts to promote drugs directly to consumers).

influence your chances of obtaining a job or a date or even interfere with your job performance?”) and suggested that consumers talk with their physicians about their hair loss.¹⁸¹ Upjohn’s campaign apparently worked—Rogaine became a widely sold drug, with global revenue estimated at 1.2 billion dollars in 2015.¹⁸² Likewise, Propecia was widely and successfully promoted DTC, becoming the second most highly promoted DTC prescription drug within just a few years of approval and reaching roughly 400 million dollars in sales per year before generic versions entered the market.¹⁸³

2. Botox

The regulatory history for Botox (onabotulinumtoxinA) is similar to that for Rogaine and Propecia in many ways, although the risks of Botox are arguably more serious than those associated with either Rogaine or Propecia. Botox was originally approved as a prescription drug for therapeutic uses—the first approved indication was for treating adult eye muscle movement disorders.¹⁸⁴ After over ten years on the market as an approved therapy,¹⁸⁵ in 2002, the FDA approved Botox, under the brand-name “Botox Cosmetic,” for “the temporary

181. Teresa Moran Schwartz, *Consumer-Directed Prescription Drug Advertising and the Learned Intermediary Rule*, 46 FOOD DRUG COSM. L.J. 829, 837 (1991).

182. *Minoxidil Market Insights*, GLOB. MKT. INSIGHTS (Nov. 2018), <https://perma.cc/NY28-XYDK>.

183. See Pines, *supra* note 179, at 507–08; Jim Edwards, *Why Merck’s Hair Loss Drug Could Make Its Income Statement Go, Um, Limp*, CBS NEWS (Jan. 13, 2011, 5:11 PM), <https://perma.cc/874A-ZPE4>.

184. See *Botox Approval History*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/4S2K-E3KL>.

185. See *id.* Following its original approval, the FDA approved Botox for additional therapeutic uses, including cervical dystonia in 2000, and then after Botox Cosmetic’s approval, severe primary axillary hyperhidrosis in 2004, upper limb spasticity and the prevention of headaches in patients with chronic migraines in 2010, urinary incontinence in 2011, overactive bladder in 2013, and lower limb spasticity in 2016. See *id.*

improvement in the appearance of moderate to severe glabellar lines” (i.e., frown lines between the eyebrows).¹⁸⁶

Botox’s use for this purpose is fairly intuitive—it is a neurotoxin that blocks nerve signals telling muscles to move, and muscle contractions cause wrinkles.¹⁸⁷ And the FDA’s 2002 approval of Botox for glabellar lines was supported by seemingly robust evidence of effectiveness. Allergan,¹⁸⁸ Botox’s manufacturer, conducted two randomized, double-blind, placebo controlled clinical trials, including a total of 537 subjects with moderate to severe frown lines.¹⁸⁹ The subjects were given Botox Cosmetic (or placebo) and rated thirty days later—by themselves and the researchers—on the severity of their wrinkles.¹⁹⁰ Significantly more subjects who received Botox Cosmetic were rated as having no lines or only mild lines at thirty days (roughly 80 percent versus 3 percent).¹⁹¹

As a neurotoxin, however, Botox is also associated with serious risks. At the time that the FDA first approved Botox for wrinkles, the drug’s FDA-approved labeling including warnings about rare cardiovascular adverse events, including potentially fatal ones, as well as the transmission of viral diseases such as Creutzfeldt-Jakob disease (CJD), a degenerative, fatal brain

186. U.S. FOOD & DRUG ADMIN., 2002 BOTOX LABELING 2 (2002), <https://perma.cc/4GWH-VN5L> (PDF). Indicative, perhaps, of the porous line between therapeutic and non-therapeutic uses, although the indication on the FDA-approved labeling does not use therapeutic terms, in the approval letter, the agency described the approved use as the “*treatment* of glabellar lines.” *Botox Cosmetic Approval Letter*, U.S. FOOD & DRUG ADMIN. (Apr. 12, 2002), <https://perma.cc/QWD4-UBZ7> (last updated Apr. 14, 2002) (emphasis added).

187. See, e.g., 2002 BOTOX LABELING, *supra* note 186, at 1.

188. Allergan is the manufacturer of many other aesthetic drugs and devices, including a dermal filler marketed as Juvederm, see *infra* Part II.A.4, as well as others not discussed in detail in this Article, such as Latisse, a prescription drug approved for eyelash growth and Kybella, a prescription drug approved for eliminating fat in the chin (i.e., eliminating a “double chin”). See, e.g., Meg Tirrell (@megtirrell), TWITTER (Sept. 14, 2018, 6:21 AM), <https://perma.cc/6TJB-F37R> (describing Allergan’s “medical aesthetics day” conference).

189. See 2002 BOTOX LABELING, *supra* note 186, at 2.

190. See *id.*

191. See *id.* at 3 (noting $p < .001$).

disorder.¹⁹² Since that original approval, additional risks have become known—including that Botox may spread from the site of injection to other areas of the body, producing symptoms of botulism, such as breathing difficulties that are potentially fatal.¹⁹³ One way the FDA manages these risks is by requiring a prescription for Botox.¹⁹⁴ Additionally, after the FDA received new authority in 2007 to require Risk Evaluation and Mitigation Strategies (REMS) for prescription drugs that pose the most serious risks, the agency required a REMS for Botox for both its therapeutic and non-therapeutic uses, which consisted primarily of patient labeling until the REMS requirement was released in 2012.¹⁹⁵ The drug’s labeling also includes a “black box warning” about its fatal risks—the kind of warning that the FDA reserves for the most serious risks associated with drugs.¹⁹⁶ None of the risks of Botox, however—including the potentially fatal ones—have led the FDA to decline to approve, or withdraw approval of, the use of Botox for glabellar lines.

Moreover, these risks did not lead the FDA to decline to approve two additional non-therapeutic uses for Botox—lateral canthal lines (i.e., crow’s feet) in 2013 and forehead lines in

192. *See id.* at 9.

193. *See, e.g.*, U.S. FOOD & DRUG ADMIN., 2009 BOTOX LABELING 1 (2009), <https://perma.cc/5BDH-6KT8> (PDF).

194. *See* U.S. FOOD & DRUG ADMIN., BOTOX LABELING 1 (2020), <https://perma.cc/TQW6-MCWC> (PDF) (detailing prescription requirements).

195. *See* U.S. FOOD & DRUG ADMIN., BOTOX APPROVAL LETTER 2–3 (2009), <https://perma.cc/GJP2-B4PS> (PDF). The decision to release the REMS requirement for Botox was consistent with the agency’s policy decision, at the time, to stop requiring REMS that primarily consist of patient labeling. But patient labeling, known as a Medication Guide, is still required for Botox. *See* U.S. FOOD & DRUG ADMIN., BOTOX RELEASE REMS REQUIREMENT LETTER 2 (2012), <https://perma.cc/5JG4-AUGW> (PDF); U.S. FOOD & DRUG ADMIN., GUIDANCE: MEDICATION GUIDES—DISTRIBUTION AND INCLUSION IN RISK EVALUATION AND MITIGATION STRATEGIES (REMS), 2–6 (2011), <https://perma.cc/BRF6-D2ZH> (PDF).

196. *See* 21 C.F.R. § 201.57(c) (2020); U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: WARNINGS AND PRECAUTIONS, CONTRAINDICATIONS, AND BOXED WARNING SECTIONS OF LABELING FOR HUMAN PRESCRIPTION DRUG AND BIOLOGICAL PRODUCTS CONTENT AND FORMAT 2 (2011), <https://perma.cc/9NBH-ZNNN> (PDF).

2017—for which the effectiveness data are similar to that for glabellar lines.¹⁹⁷ Although health care professionals could, and undoubtedly did, provide Botox for these purposes before the FDA approvals, Allergan, nevertheless, undertook the clinical trials necessary to assess the drug's safety and effectiveness for these uses, to obtain the FDA's approval.¹⁹⁸ That investment—as well as DTC advertising campaigns, which recently have begun to target men as well as women—seemingly has paid off.¹⁹⁹ By 2006, yearly sales of Botox were over \$1 billion with approximately half due to cosmetic uses.²⁰⁰ By 2013, yearly sales were over \$2 billion and the continued pursuit of new uses for Botox was perceived as a key driver of Allergan's overall value.²⁰¹

3. Breast Implants

Breast implants provide an example of devices that the FDA has approved for a non-therapeutic use, and the long, controversial regulatory history—particularly for silicone breast implants—offers a few insights into the FDA's approach to non-therapeutic uses.²⁰² Although breast implants have been

197. See U.S. FOOD & DRUG ADMIN., BOTOX APPROVAL LETTER 1 (2013), <https://perma.cc/D9FJ-9XS2> (PDF); U.S. FOOD & DRUG ADMIN., BOTOX APPROVAL LETTER 1 (2017), <https://perma.cc/TNV9-TKAX> (PDF).

198. See U.S. FOOD & DRUG ADMIN., 2013 BOTOX LABELING 10 (2013), <https://perma.cc/YC7V-ZKEL> (PDF). It is, perhaps, worth noting that Allergan challenged the FDA's policies restricting off-label promotion of Botox on First Amendment grounds, although Allergan withdrew its lawsuit as part of a settlement. See Complaint at 26–38, *Allergan v. United States*, No. 09-01879 (D.D.C. Oct. 14, 2010) (dismissed per stipulation).

199. See Aliko Carter, *Deion Sanders Loves BOTOX and Is Getting His Message Out to Men*, FORBES (Jan. 15, 2018), <https://perma.cc/H2PB-PGU6>.

200. See Emilia Petrarca, *On the 15th Anniversary of Botox, an Appreciation of How It's Changed Everyone*, W MAG. (Apr. 14, 2017), <https://perma.cc/49YS-K6VQ>.

201. See Joseph Walker, *Botox Itself Aims Not to Age*, WALL ST. J. (May 18, 2014), <https://perma.cc/KNC6-5QKH>.

202. See, e.g., MARCIA ANGELL, SCIENCE ON TRIAL: THE CLASH OF MEDICAL EVIDENCE AND THE LAW IN THE BREAST IMPLANT CASE, 54–57 (1996); Dresser et al., *supra* note 7, at 706; David E. Bernstein, *The Breast Implant Fiasco*, 87

on the market since the early 1960s, Congress did not create the modern scheme for FDA regulation of devices until 1976 and the FDA did not require breast implant manufacturers to submit PMAs until 1991.²⁰³ Today there are over two hundred PMAs approved for breast implants.²⁰⁴ Like hair growth drugs and Botox, the FDA has approved breast implants for both therapeutic and non-therapeutic uses—but for breast implants the agency has more clearly appeared to weigh the value of the product’s therapeutic and non-therapeutic benefits differently.²⁰⁵

The FDA approved the first PMAs for breast implants in 2000.²⁰⁶ The applications covered saline breast implants intended both for aesthetic uses and for therapeutic reconstruction following medically necessary mastectomies.²⁰⁷ At the time of approval, the FDA judged the implants—whether intended for aesthetic or reconstructive purposes—to be associated with various risks, including serious risks such as the need for additional surgery over the course of the recipient’s life.²⁰⁸ The FDA, however, judged the benefits of both the aesthetic and reconstructive uses to outweigh these risks, provided certain conditions—such as conducting a ten-year post-approval follow-up study—were met.²⁰⁹

CAL. L. REV. 457, 459–60 (1999); *Regulatory History of Breast Implants in the U.S.*, *supra* note 11.

203. See *Regulatory History of Breast Implants in the U.S.*, *supra* note 11.

204. See *Premarket Approval (PMA) Database*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/JA4L-L2LX> (last updated Oct. 12, 2020) (yielding roughly 230 approved applications when searching for “breast implant” in the FDA’s PMA database).

205. See, e.g., Mehlman, *supra* note 24, at 702.

206. See *Regulatory History of Breast Implants in the U.S.*, *supra* note 11.

207. See *id.* Allergan, the manufacturer of Botox, was also the manufacturer of one of the first approved breast implants. See *Premarket Approval of Natrelle Saline Breast Implants*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/F2FX-YTHL> (last updated Oct. 19, 2020).

208. See U.S. FOOD & DRUG ADMIN., SUMMARY OF SAFETY AND EFFECTIVENESS DATA OF SALINE-FILLED MAMMARY PROSTHESIS 4 (2000), <https://perma.cc/ZX5A-CYT2> (PDF).

209. See, e.g., U.S. FOOD & DRUG ADMIN., NATRELLE APPROVAL ORDER 1 (2000), <https://perma.cc/E64E-XG74> (PDF).

This is not to say that the agency judged the benefits of non-therapeutic uses as equal to those of therapeutic uses. Until 2006, the FDA authorized only the reconstructive, but not the aesthetic, use of *silicone* breast implants—which at the time were thought to be associated with risks greater than those associated with saline implants.²¹⁰ This different approach likely reflected the FDA's view that those potential greater risks were outweighed by reconstructive but not aesthetic benefits.²¹¹

4. Dermal Fillers

As with breast implants, the FDA—since the early 1980s—has approved as devices dozens of dermal fillers, under brand-names such as Restylane and Juvederm.²¹² Dermal fillers typically consist of materials such as collagen or hyaluronic acid that are injected into the body to smooth wrinkles or add volume to the skin.²¹³ Although dermal fillers are injectable products, they are regulated as devices, rather than drugs,

210. See *Regulatory History of Breast Implants in the U.S.*, *supra* note 11; see also Mehlman, *supra* note 24, at 702 (explaining the FDA's decision to limit research of silicone gel-filled implants to reconstructive purposes). Some concerns about silicone breast implants being associated with, for example, autoimmune disorders were ultimately not borne out. See, e.g., Bernstein, *supra* note 202, at 484; Dresser et al., *supra* note 7, at 743. The aesthetic indication for the saline breast implants also was limited to adults, whereas the indication for reconstruction was not, suggesting that the FDA may have weighed the two uses differently. See SUMMARY OF SAFETY AND EFFECTIVENESS DATA OF SALINE-FILLED MAMMARY PROSTHESIS, *supra* note 208, at 1 (listing indications for use). On the other hand, the differing indications may simply reflect the rarity with which reconstruction likely occurs in minors.

211. See Mehlman, *supra* note 24, at 702.

212. A search for “dermal filler” in the FDA's PMA database yields sixty-four approved applications. *Premarket Approval (PMA) Database*, *supra* note 204.

213. See, e.g., U.S. FOOD & DRUG ADMIN., RESTYLANE LABELING 1 (2016), <https://perma.cc/A9UY-4NJD> (PDF); *Dermal Fillers Approved by the Center for Devices and Radiological Health*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/9S6H-XK82> (last updated Aug. 29, 2018).

because they work primarily through physically filling the skin rather than through chemical action.²¹⁴

Like many non-therapeutic uses of drugs, the FDA determined that at least some dermal fillers are effective based on clinical trials assessing both researchers' and subjects' own judgments that the dermal fillers had reduced the appearance of wrinkles.²¹⁵ Also like both breast implants and non-therapeutic uses of drugs, dermal fillers are not risk-free. The most common adverse events are relatively minor, including bruising, pain, and redness.²¹⁶ They, however, also are associated with serious risks, such as necrosis and anaphylactic shock, as well as aesthetic adverse effects, such as movement of the filler or the formation of permanent, hard nodules on the skin.²¹⁷ Consistent with these risks, the FDA restricts dermal fillers to prescription use.²¹⁸

Moreover, the FDA's approval decisions for dermal fillers provide some evidence the FDA also judges the risks and benefits of different non-therapeutic uses differently. For example, the FDA first approved a permanent, rather than a temporary, dermal filler in 2006 only for one non-therapeutic use in patients over twenty-one years of age—nasolabial folds (wrinkles on the side of the mouth that extend upward toward the nose)—but not for the other non-therapeutic uses for which temporary dermal fillers are approved, such as lip and cheek augmentation.²¹⁹ Permanent dermal fillers pose similar risks to

214. See 21 U.S.C. § 321(g)(1), (h); see also *Genus Med. Techs., LLC v. FDA*, 427 F. Supp. 3d 74, 77 (D.D.C. 2019) (describing the drug and device definitions); Lars Noah, *Growing Organs in the Lab: Tissue Engineers Confront Institutional "Immune" Responses*, 55 JURIMETRICS J. 297, 314 n.93 (2015) ("The FDA regulates some injectable products as medical devices." (citation omitted)).

215. See, e.g., RESTYLANE LABELING, *supra* note 213, at 1.

216. See *Dermal Fillers (Soft Tissue)*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/9CY5-JGD3> (last updated Nov. 26, 2018).

217. See *id.*

218. See U.S. FOOD & DRUG ADMIN., RESTYLANE APPROVAL ORDER 1 (2016), <https://perma.cc/ZFT7-9KS2> (PDF).

219. See U.S. FOOD & DRUG ADMIN., ARTEFILL LABELING 1 (2006), <https://perma.cc/2C9Q-3TRL> (PDF); *Dermal Fillers (Soft Tissue)*, *supra* note 216. Artefill, now marketed as Bellafill, is described as permanent because it is

temporary dermal fillers but, because of their permanence, certain adverse effects, such as lumps—or simply dissatisfaction with the results—are more difficult to address.²²⁰ In 2014, the FDA also approved an arguably-therapeutic use for the permanent dermal filler (filling acne scars in people over twenty-one years of age), underscoring the links between therapeutic and non-therapeutic uses and showing that therapeutic uses might sometimes follow non-therapeutic ones.²²¹

IV. CONTEMPLATING THE FUTURE

As a descriptive matter, the FDCA gives the FDA significant latitude to determine whether a particular product use is safe and effective, and FDA review of the safety and effectiveness of non-therapeutic uses has not proven to be an impossible impediment to their marketing. But that still leaves question of whether it *should*.²²² This Part argues, first, that this question may become more salient, as changes in technology, law, and policy are poised to force the FDA to more frequently

made of non-absorbable polymethylmethacrylate beads, rather than absorbable collagen or hyaluronic acid, and has been shown to last at least five years in clinical trials. ARTEFILL LABELING, *supra*, at 1.

220. See *Dermal Fillers (Soft Tissue)*, *supra* note 216.

221. See U.S. FOOD & DRUG ADMIN., BELLAFILL LABELING 1 (2014), <https://perma.cc/5V6Y-TXGY> (PDF); see also Joan Kron, *This New Filler Is a Game Changer*, ALLURE (Sept. 10, 2015), <https://perma.cc/5WXK-FCTT> (explaining how Bellafill works to fill smile lines and acne scars).

222. There may be relevant normative questions in addition to the question of whether the FDA should be willing to use its discretion to conclude that non-therapeutic uses are safe and effective, such as what *kinds* of information are appropriate for the FDA to consider in assessing benefits and risks. See, e.g., Konnoth, *supra* note 151, at 187. Moreover, there may be important practical questions about the FDA's institutional norms and resources. For example, there may be questions about whether the FDA's current scientific staff have the expertise to review the safety and effectiveness of recreational and enhancing non-therapeutic uses, with which the agency does not have the same amount of experience as it does with aesthetic uses. Cf. *id.* at 219 (addressing arguments that the FDA lacks expertise to address certain kinds of "side effects" of drugs).

confront its possible authority over not just aesthetic uses of drugs and devices, but also recreational or enhancing uses.²²³

This Part then begins to explore the normative question of how the FDCA's safety and effectiveness standard should be applied to non-therapeutic uses. It considers several of the purposes that FDA approval serves—an analysis that preliminarily suggests the agency could reasonably take various different approaches to assessing the safety and effectiveness of non-therapeutic uses. This, in turn, provides further support for the Article's claim that arguments grounded in the idea that the FDCA's safety and effectiveness standards would necessarily ban non-therapeutic uses will not be useful tools for determining the scope of FDA jurisdiction.

A. *Beyond Aesthetic Uses*

Non-therapeutic uses of drugs and devices are nothing new.²²⁴ For centuries, humans have used caffeine and ginkgo biloba to improve energy, focus, or memory, equipment and chemical interventions to improve athletic performance, and numerous substances, such as cocaine and psychedelics, recreationally.²²⁵ As Part III shows, the FDA has long regulated aesthetic uses of drugs and devices.²²⁶ Against this background one might wonder why consider the FDA's jurisdiction over non-therapeutic uses particularly at a time when the COVID-19 pandemic is highlighting pressing questions about the agency's application of its drug and device authorities to desperately-needed therapeutic uses during public health emergencies.²²⁷ But the time is, arguably, ripe to consider the

223. See, e.g., Patricia J. Zettler & Erika Lietzan, *A Special Exception for CBD in Foods and Supplements?*, 25 DRUG DISCOVERY TODAY 467, 467 (2020) (discussing the increased relevance of FDA jurisdiction over aspects of the cannabis industry).

224. See, e.g., Maxwell J. Mehlman, *Cognition-Enhancing Drugs*, 82 MILBANK Q. 483, 484 (2004).

226. See, e.g., *id.*

226. See *supra* Part III.

227. For a small selection of some recent scholarship discussing the FDA's approach to drugs, vaccines, and devices intended to treat, prevent, or diagnose COVID-19, see Jerry Avorn & Aaron S. Kesselheim, *Up Is Down—*

future of non-therapeutic uses because evolutions in technology, as well as in law and policy, appear poised to create markets of non-therapeutic uses that will more frequently intersect with the FDA's drug and device powers.²²⁸

For example, some hope that emerging technologies may prove to be better—safer or more effective—for non-therapeutic uses than existing technologies have been.²²⁹ At the same time, at least some novel non-therapeutic technologies may be challenging to legally market without FDA authorization. Human genome editing provides a dramatic example.²³⁰ After decades of work to develop gene therapies, newer techniques, such as CRISPR, have made genome editing easier and cheaper to carry out.²³¹ Genetic interventions hold promise for both therapeutic and non-therapeutic uses. A genetic intervention that effectively builds muscle might treat patients with

Pharmaceutical Industry Caution vs. Federal Acceleration of COVID-19 Vaccine Approval, 383 NEJM 1706 (2020); Evans & Clayton, *supra* note 6; Ameet Sarpatwari et al., *Missed Opportunities on Emergency Remdesivir Use*, 324 JAMA 331 (2020); Benjamin N. Rome & Jerry Avorn, *Drug Evaluation During the COVID-19 Pandemic*, 392 NEJM 2282 (2020); Parasidis et al., *supra* note 152; Yaniv Heled et al., *Regulatory Reactivity: FDA and the Response to COVID-19*, FOOD & DRUG L.J. (forthcoming 2021) (on file with author); Jacob S. Sherkow, *Regulatory Sandboxes and the Public Health* (in progress) (on file with author).

228. Cf. Taleed El-Sabawi, *Why the DEA, Not the FDA? Revisiting the Regulation of Potentially-Addictive Substances*, 16 N.Y.U. J.L. & BUS. 317, 321 (2020) (analyzing the history of FDA authority over “illicit sales of non-narcotic drugs, like barbiturates and amphetamines”); Max A. Cherney, *Tilray Partners with Novartis in Big Pharma's First Deal of its Kind with Big Marijuana*, MARKETWATCH (Dec. 18, 2018, 10:16 AM), <https://perma.cc/YF64-5YDU> (PDF) (describing Novartis's partnership with a medical cannabis company).

229. Many FDA-regulated products that traditionally have been popular for non-therapeutic purposes have been ineffective or unsafe. For instance, a dietary supplement company conducted a study comparing the cognitive enhancing effects of coffee with that of its own so-called “nootropic” supplement—and found that coffee worked better than its own product. See Chrissy Farr, *This Start-Up Raised Millions to Sell 'Brain-Hacking' Pills, but its Own Study Found Coffee Works Better*, CNBC (Nov. 30, 2017, 4:02 PM), <https://perma.cc/PQ56-53R6>.

230. See NAT'L ACADS. OF SCIS., ENG'G & MED., *supra* note 15, at 137.

231. See, e.g., Jacob S. Sherkow et al., *Is It 'Gene Therapy'?* 5 J.L. & BIOSCIENCES 786, 789 (2018).

muscular dystrophy *and* be used for healthy individuals interested in enhancing physical performance.²³² But this example of overlapping therapeutic and non-therapeutic uses is likely to be rare because “the specificity of edited cells will make [off-label] applications less likely” than for traditional drugs and devices—making any non-therapeutic uses more likely to be subject to the FDA’s premarket review requirements.²³³ Moreover, because of the potential serious risks associated with genetic interventions, the FDA may be unlikely to decline to enforce premarket review requirements for such uses.²³⁴

Perhaps more importantly, changes to the FDCA, as well as to other areas of law and policy, also may lead to non-therapeutic uses more frequently coming before the FDA. An example involving the FDCA comes from the 21st Century Cures Act of 2016.²³⁵ That law amended the FDCA to ease the development of new uses of already approved products—such as the use of Botox for wrinkles, when the drug was already approved for therapeutic uses.²³⁶ Specifically, the FDCA now permits the FDA to consider “real world evidence,” including “data . . . from sources other than randomized clinical trials,” such as from clinical practice,²³⁷ when evaluating new uses of already approved products.²³⁸ Manufacturers may be more likely to seek FDA approval of non-therapeutic drug uses if this provision enables approval of such uses without expensive clinical trials, but instead based on experience in clinical practice—such as the evidence that patients using Rogaine’s active ingredient for hypertension also experienced hair

232. See NAT’L ACADS. OF SCIS., ENG’G & MED., *supra* note 15, at 9.

233. *Id.* at 152; see *supra* Part II.C (discussing the regulatory regime for off-label uses).

234. Cf. *Information about Self-Administration of Gene Therapies*, U.S. FOOD & DRUG ADMIN. (Nov. 21, 2017), <https://perma.cc/H6X4-55BR> (cautioning consumers on the risks of do-it-yourself gene therapies).

235. Pub. L. No. 114-255 § 3022, 130 Stat. 1033 (2016).

236. See *supra* Part III.B.2.

237. 21 U.S.C. § 355g(b).

238. See 21st Century Cures Act, Pub. L. No. 114-255 § 3022, 130 Stat. 1033; Jordan Paradise, *21st Century Citizen Pharma: The FDA & Patient-Focused Product Development*, 44 AM. J.L. & MED. 309, 310 (2018).

growth.²³⁹ The 21st Century Cures Act also amended the FDCA to encourage the FDA to incorporate “patient experience data” into its evaluations, which may further ease the development of non-therapeutic uses for which patient self-assessments are important indicators of effectiveness.²⁴⁰

Likewise, legal developments not directly tied to the FDA’s enabling statutes also may bring new non-therapeutic uses before the agency. Most notably, widespread state level cannabis decriminalization (or de facto decriminalization) has allowed quasi-legal markets to emerge.²⁴¹ Both the FDA and the traditional pharmaceutical industry have paid increasing attention to cannabis products, albeit with a primary focus on therapeutic uses of such products.²⁴² But particularly now that

239. See Rachel E. Sherman et al., *Real-World Evidence—What Is It and What Can It Tell Us?*, 375 NEW ENG. J. MED. 2293, 2296 (2016); Jonathan P. Jarow et al., *Multidimensional Evidence Generation and FDA Regulatory Decision Making: Defining and Using “Real-World” Data*, 318 J. AM. MED. ASS’N 703, 704 (2017); U.S. FOOD & DRUG ADMIN., USE OF REAL-WORLD EVIDENCE TO SUPPORT REGULATORY DECISION-MAKING FOR MEDICAL DEVICES: GUIDANCE FOR INDUSTRY AND FOOD AND DRUG STAFF 8 (2017), <https://perma.cc/8CWF-XB6D> (PDF); U.S. FOOD & DRUG ADMIN., SUBMITTING DOCUMENTS USING REAL-WORLD DATA AND REAL-WORLD EVIDENCE TO FDA FOR DRUGS AND BIOLOGICS: DRAFT GUIDANCE FOR INDUSTRY (2019), <https://perma.cc/87AC-6RD4> (PDF); see also Jenny Bryan, *How Minoxidil Was Transformed From an Antihypertensive to Hair-Loss Drug*, PHARM. J. (July 20, 2011), <https://perma.cc/V93D-5BQW> (describing the active ingredient in Rogaine’s evolution from a hypertension treatment to a drug for hair growth); W. Nicholson Price II, *Drug Approval in a Learning Health System*, 102 MINN. L. REV. 2413, 2462 (2018) (“[I]f FDA learns more about drugs based on how they work in the real world, that information should be used to address how drugs are labeled, sold, and used.”). On the other hand, if the FDA loosens its restrictions on off-label promotion—because of First Amendment jurisprudence or for other reasons—manufacturers may have fewer incentives to seek FDA authorization of non-therapeutic uses for already-approved drugs and devices. See, e.g., FDA MEMO, *supra* note 21, at 1; Kapczynski, *supra* note 21, at 2359; see also Lietzan, *supra* note 162, at 171–83 (describing the process and incentives for developing new uses).

240. See Paradise, *supra* note 238, at 321–22.

241. See, e.g., Kamin, *supra* note 15, at 624; Robert A. Mikos, *Marijuana Localism*, 65 CASE W. RESV. L. REV. 719, 767 (2015).

242. See U.S. FOOD & DRUG ADMIN., CANNABIS AND CANNABIS-DERIVED COMPOUNDS: QUALITY CONSIDERATIONS FOR CLINICAL RESEARCH: GUIDANCE FOR

at least eleven states and the District of Columbia have decriminalized adult recreational use of cannabis,²⁴³ in the near future the FDA may face questions about its authority over recreational cannabis products.²⁴⁴ Indeed, as of the time of writing, the most recent federal bill to propose decriminalizing cannabis at the federal level expressly stated that it would not “affect or modify” the FDCA.²⁴⁵

Questions about FDA jurisdiction over recreational uses of substances other than cannabis are likely to arise as well. Since 2018, Ann Arbor, Denver, Oakland, Santa Cruz, and Washington, D.C. have established policies that effectively decriminalize certain uses of psychedelic substances, such as psilocybin.²⁴⁶ Additionally, in November 2020, Oregon voters passed one initiative that permits the therapeutic use of psilocybin under certain conditions and one that de facto decriminalizes possession small amounts of all drugs.²⁴⁷ In the

INDUSTRY (2020), <https://perma.cc/XD8T-L5XA> (PDF); Cherney, *supra* note 228; O'Connor & Lietzan, *supra* note 71, at 850.

243. *Marijuana Overview*, NAT'L CONF. ON STATE LEGISLATURES (Oct. 17, 2019), <https://perma.cc/V43T-FLRP>.

244. *Cf.* O'Connor & Lietzan, *supra* note 71, at 902–03 (speculating how cannabis products intended for recreational use might be treated by the FDA).

245. Marijuana Opportunity Reinvestment and Expungement Act of 2020, H.R. 3884, 116th Cong., <https://perma.cc/RD75-UXAS>.

246. *See* Mason M. Marks, *Controlled Substance Regulation for the Covid-19 Mental Health Crisis*, 72 ADMIN. L. REV. 649, 654 (2020) (noting Denver, Oakland, Santa Cruz, and Washington, D.C.'s de facto decriminalization policies); *Ann Arbor Decriminalizes Magic Mushrooms, Psycheogenic Plants*, A.P. NEWS (Sept. 26, 2020), <https://perma.cc/T22E-GCYM> (PDF); *see also* Dustin Marlan, *Beyond Cannabis: Psychedelic Decriminalization and Social Justice*, 23 LEWIS & CLARK L. REV. 851, 872 (2019) (“We are now beginning to see the decriminalization of psychedelics, namely psilocybin, at the state and municipal levels as well.”).

247. *Oregon Measure 109, Psilocybin Mushroom Services Program Initiative (2020)*, BALLOTPEdia, <https://perma.cc/23L9-QMAW>; *Oregon Measure 110, Drug Decriminalization and Addiction Treatment Initiative (2020)*, BALLOTPEdia, <https://perma.cc/WZ6S-NAB2>; *see* Cleve R. Wootson, Jr. & Jaclyn Peiser, *Oregon Decriminalizes Possession of Hard Drugs, As Four Other States Legalize Recreational Marijuana*, WASH. POST (Nov. 4, 2020), <https://perma.cc/PS9L-UU8R> (“Oregon voters approved a controversial ballot measure decriminalizing possession of small amounts of so-called hard drugs, including cocaine, heroin, oxycodone and methamphetamines.”).

wake of these changes, some are predicting the psychedelic market will explode, which, in turn, could raise questions about FDA jurisdiction over recreational uses of these substances.²⁴⁸

B. *Considering the Purposes of Safety and Effectiveness Review*

If technological, legal, and policy developments do in fact give rise to more, or new, non-therapeutic uses that potentially intersect with FDA jurisdiction, the FDA will be faced with both a legal question about whether it can regulate such technologies under its drug and device authorities, and also, if it can, how it should apply the statutory standards for safety and effectiveness to such uses. To begin to examine that question, this section considers three of the public health purposes the FDA's premarket approval processes for drugs and devices are thought to serve: protecting people from unsafe and ineffective products, addressing information asymmetries between people and manufacturers, and incentivizing the development of socially valuable information.²⁴⁹ This analysis suggests that there are arguments that finding non-therapeutic uses to be safe and effective, or taking a flexible approach to such assessments, may be a normatively permissible approach for the agency.²⁵⁰

248. See *North American Psychedelic Drugs Market Could Exceed \$6.8 Billion by 2021*, FIN. NEWS MEDIA (Jan. 6, 2021), <https://perma.cc/7GVK-Y4WG>.

249. See, e.g., FDA Memo, *supra* note 21; Eisenberg, *The Role of the FDA in Innovation Policy*, *supra* note 21, at 361; Kapczynski, *supra* note 21, at 2360; Ariel Katz, *Pharmaceutical Lemons: Innovation and Regulation in the Drug Industry*, 14 MICH. TELECOMM. & TECH. L. REV. 1, 13 (2007); cf. President John F. Kennedy, Special Message to the Congress on Protecting the Consumer Interest (Mar. 15, 1962), <https://perma.cc/2WJS-QP7R> (describing four consumer rights: the right to safety, the right to be informed, the right to choose, and the right to be heard).

250. To be clear, this Article does intend to affirmatively argue that any safety and effectiveness determinations for specific products were correct (or incorrect), nor that the overall approach that the FDA has seemingly adopted for assessing the benefits and risks of aesthetic uses is the best one. Instead, this Part aims to show that the range of approaches the agency could reasonably take to assess the safety and effectiveness of non-therapeutic uses

1. Protecting People from Unsafe and Ineffective Products

The traditional rationale for requiring the FDA's premarket review of drug and device safety and effectiveness is protecting people from unsafe and ineffective products.²⁵¹ Considering this purpose, Rachel Sachs has explained that one way to conceptualize the FDA's task is that, in implementing its premarket approval processes, the FDA must balance the risk of making Type I errors—in which the agency authorizes an unsafe or ineffective use of a drug or device—against the risk of making Type II errors—in which the agency fails to authorize a safe and effective use of a drug or device.²⁵² Making too many Type I errors will subject patients and consumers to harmful uses of products and undermine public trust in the agency.²⁵³ Making too many Type II errors would deny patients access to often desperately needed therapies.²⁵⁴ And there have long been differing views about whether the FDA generally is striking the right balance between Type I and Type II errors for therapeutic uses.²⁵⁵ Some have argued that the FDA may set the bar for demonstrating safety and effectiveness too low,²⁵⁶ while others, for example, have argued for open access to therapeutic uses on the ground that patients have a protected liberty interest in

is at least arguably broad. This in turn provides additional evidence against arguments that the FDCA would categorically preclude the agency from finding non-therapeutic uses safe and effective.

251. See, e.g., Eisenberg, *The Role of the FDA in Innovation Policy*, *supra* note 21, at 345.

252. See, e.g., Rachel E. Sachs, *Delinking Reimbursement*, 102 MINN. L. REV. 2307, 2323–24 (2018).

253. See *id.* at 2323.

254. See *id.* at 2324.

255. See, e.g., Robert Kemp & Vinay Prasad, *Surrogate Endpoints in Oncology: When Are They Acceptable for Regulatory and Clinical Decisions, and Are They Currently Overused?* 15 BMC MED., NO. 15, 2017, at 5; Nicholas S. Downing et al., *Clinical Trial Evidence Supporting FDA Approval of Novel Therapeutics, 2005–2012*, 311 JAMA 368, 372–73 (2014); C. Frederick Beckner, III, Note, *The FDA's War on Drugs*, 82 GEO. L.J. 529, 531 (1993).

256. See, e.g., Kemp & Prasad, *supra* note 257, at 5.

accessing medical interventions regardless of whether the FDA has authorized their use (albeit without success in the courts).²⁵⁷

Similarly, the question of how to strike the balance between Type I and Type II errors in the context of non-therapeutic uses might lend itself to differing views. Arguably, avoiding Type I errors is more important for non-therapeutic than therapeutic uses.²⁵⁸ Under this view, because the benefits of a non-therapeutic use are inherently less than those of a therapeutic use, the risks of a non-therapeutic use should be quite low, or the benefits quite high (or both), for the FDA to determine that the use has a favorable benefit-risk balance.²⁵⁹ That is, the FDA should err on the side of protecting consumers from risky and ineffective non-therapeutic uses, particularly where consumers do not have the same strong interest in access that terminally and seriously ill patients do.²⁶⁰ This might lead the FDA, for example, to refuse to approve Botox and dermal fillers for aesthetic uses because of the risk of death associated with both—even if rare.²⁶¹

By contrast, minimizing Type I errors might be *less* important, or at least no more important, for non-therapeutic than for therapeutic uses.²⁶² For therapeutic uses, patients may not have much choice as to whether to use a particular drug or

257. See *Abigail All. for Better Access to Developmental Drugs v. von Eschenbach*, 495 F.3d 695, 711 (D.C. Cir. 2007) (en banc) (finding no protected liberty interest to use experimental drugs); see also Seema Shah & Patricia Zettler, *From a Constitutional Right to a Policy of Exceptions: Abigail Alliance and the Future of Access to Experimental Therapy*, 10 *YALE J. HEALTH POL'Y, L., & ETHICS* 135, 141 (2010) (analyzing the *Abigail Alliance* decision).

258. Cf. *supra* Part III.B.3 (describing the FDA's differing evaluations of therapeutic and non-therapeutic uses of silicone breast implants).

259. See *Legitimate Medicine*, *supra* note 25, at 442.

260. Cf. Leah Isakov et al., *Is the FDA Too Conservative or Too Aggressive? A Bayesian Decision Analysis of Clinical Trial Design*, 211 *J. ECONOMETRICS* 117, 128 (2019) (positing that traditionally accepted proportions of Type I error are too conservative for drugs treating terminal illnesses, but too large in other instances).

261. See *supra* Part III.

262. Cf. *What Lies Ahead*, *supra* note 22, at 321 (raising this argument as a possibility). The analysis in Part III suggests this view might be more consistent with the approach the FDA has actually adopted for assessing safety and effectiveness of aesthetic uses.

device as a practical matter—there may be only one therapy for their disease or condition, or their choice may be dictated by their physician’s or insurer’s views.²⁶³ Thus, *patients* might merit a high level of protection from dangerous or ineffective therapies that, in essence, their disease or condition would force them to take (and that the health care system would be forced to pay for).²⁶⁴ *Consumers*, on the other hand, who voluntarily engage in non-therapeutic uses may be in need of less protection (assuming a free choice, including a non-addictive product).²⁶⁵ Consistent with this idea, numerous kinds of consumer products outside of the FDA’s jurisdiction—including those that can cause grave harm—may be marketed without a premarket review process.²⁶⁶ Accordingly, once some minimal threshold of safety and effectiveness is cleared, perhaps consumers should be able to choose to use non-therapeutic technologies, like hair

263. Cf. Pauline Bartolone, *Behind the EpiPen Monopoly: Lobbying Muscle, Flailing Competition, Tragic Deaths*, KHN (Sept. 8, 2016), <https://perma.cc/4H7A-AYKR> (discussing a period when there was no alternative to Mylan’s EpiPen for treating anaphylactic shock).

264. See Scott Gottlieb, Comm’r, U.S. Food & Drug Admin., Speech: Capturing the Benefits of Competition for Patients (Mar. 7, 2018), <https://perma.cc/A7RW-5EFK> (“Is a patient really in a position to make an economically-based decision? . . . Of course not.”); see also Sachs, *supra* note 252, at 2309 (“In the United States, federal law requires Medicare and Medicaid to cover most, and in many cases all, FDA-approved drugs.”).

265. See *What Lies Ahead*, *supra* note 22, at 322 (suggesting that consumers need less protection). The assumption of a free choice may only rarely be a fair one. Some of the social or ethical concerns about non-therapeutic uses involve the idea that consumers will not be able to freely choose to engage in or decline such uses. For example, some have argued that consumers will not or do not freely choose aesthetic changes or enhancement, but instead opt to alter their appearance or enhance performance because of societal pressure to do so. See, e.g., Nicholas S. Fitz et al., *Public Attitudes Toward Cognitive Enhancement*, 7 *NEUROETHICS* 173, 178 (2013).

266. Cf. Noah, *supra* note 14, at 5–9 (considering the possibility of FDA regulation of firearms, given the “ceaseless casualties” associated with them); Peter Yankowski, *Police: Newtown Man Killed in Saw Accident While Clearing Tree*, *NEWTIMES*, <https://perma.cc/6HRH-VFPL> (last updated Aug. 7, 2020, 10:23AM) (documenting the tragic death of a man who accidentally killed himself with a saw).

growth drugs, cognitive enhancements, and recreational cannabis, so long as they are informed of the relevant risks.²⁶⁷

Similarly, minimizing Type II errors may be either more (or equally) important, or less important, for non-therapeutic uses as for therapeutic ones. There is a long-standing, and strongly held belief among some in the United States that people have a right to choose potentially therapeutic interventions without government interference.²⁶⁸ A belief in such freedom of choice may apply more forcefully for non-therapeutic uses, where justifications for robust FDA gatekeeping may not persuade even some who endorse the agency's role in the context of therapeutic uses.²⁶⁹ This, in turn, would suggest that avoiding Type II errors is equally, if not more, important for non-therapeutic uses compared to therapeutic ones.

Conversely, virtually all stakeholders agree that safe and effective therapies for patients, and particularly terminally and seriously ill patients, should reach the market as quickly as possible.²⁷⁰ The disagreement lies primarily in how much and what kinds of evidence are needed before such products are

267. There also may be pragmatic reasons for the FDA to be less concerned about Type I errors for non-therapeutic uses than for therapeutic uses. For example, agencies might elect to regulate cautiously or not at all to "avoid backlash and to preserve their own political capital." That is, rather than interpret the FDCA's safety and effectiveness standards as setting a high bar for non-therapeutic uses, the FDA might want to preserve political capital for fights other important public health matters. Sharon B. Jacobs, *The Administrative State's Passive Virtues*, 66 ADMIN. L. REV. 565, 623 (2014); cf. William W. Buzbee, *Recognizing the Regulatory Commons: A Theory of Regulatory Gaps*, 89 IOWA L. REV. 1, 4 (2003) (discussing issues of government regulation generally).

268. See Lewis A. Grossman, *The Origins of American Health Libertarianism*, 13 YALE J. HEALTH POL'Y, L. & ETHICS 76, 80 (2013) ("[S]truggles for freedom of therapeutic choice have recurred throughout American history.").

269. Cf. L.O. Gostin & K.G. Gostin, *A Broader Liberty: JS Mill, Paternalism and the Public's Health*, 123 PUB. HEALTH 214, 216–19 (2009) (describing some paternalistic justifications for public health regulations).

270. Cf. Shah & Zettler, *supra* note 257, at 195–96 (asserting that terminally and seriously ill patients can have compelling claims for accessing unapproved drugs while arguing against widespread access outside clinical trials).

marketed (i.e., in how to operationalize “safe and effective” and “as quickly as possible”).²⁷¹ But the same likely cannot be said of denying or delaying access to non-therapeutic uses, like aesthetic breast implants. Such a denial or a delay might be in tension with principles of individual autonomy. But it would not cause death, worsening of illness, or other tangible physical harm to a person. Moreover, limiting access to non-therapeutic uses may not as easily give rise to the arguments rooted in individual liberty interests that terminally ill patients have asserted when seeking access to experimental interventions for therapeutic purposes.²⁷² Thus, considering various views on minimizing Type I or Type II errors for non-therapeutic uses, demonstrates that the FDA arguably would be justified in adopting varied approaches to assessing such uses’ safety and effectiveness.

2. Addressing Information Asymmetries

Another purpose that the FDA’s premarket approval processes can serve is addressing information asymmetries between people and manufacturers.²⁷³ Drugs and devices are described as “credence goods,” meaning their safety,

271. See articles cited *supra* note 255 (citing differing opinions on the appropriate level of evidence needed before FDA approval).

272. Cf. Shah & Zettler, *supra* note 257, at 141 (examining the argument that terminally and seriously ill patients have a liberty interest accessing experimental interventions). If certain non-therapeutic uses, and in particular enhancing uses, become widespread such that they create a “new normal,” problems of access may become more important. For example, if only wealthy individuals can access highly effective cognitive enhancers, that could reify or exacerbate societal inequalities. See Anita L. Allen & Nicolle K. Strand, *Cognitive Enhancement and Beyond: Recommendations from the Bioethics Commission*, 19 *TRENDS COGNITIVE SCI.* 549, 551 (2015). Such access problems, however, typically are not about the initial question of FDA authorization based on safety and effectiveness—but on how technologies are distributed once demonstrated safe and effective. Cf. *Development & Approval Process | Drugs*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/BR2X-X5FK> (last updated Oct. 28, 2019) (outlining the FDA drug approval process and making no assertions about drug accessibility or price).

273. See HENRY G. GRABOWSKI & JOHN M. VERNON, *THE REGULATION OF PHARMACEUTICALS* 7 (1983); Katz, *supra* note 249, at 13–17; Kapczynski, *supra* note 21, at 2358.

effectiveness, and quality cannot be readily and easily evaluated by the people using them.²⁷⁴ For example, patients can recover from many diseases and conditions without treatment—if a patient with symptomatic COVID-19 takes a drug to treat the condition and then recovers, they, cannot, individually determine whether the recovery is due to the drug or because they were among those who would recover from COVID-19 without the drug. The FDA's premarket review of drug and device safety and effectiveness, thus, “protect[s] the misinformed [or uninformed] consumer from better-informed sellers.”²⁷⁵ As with protecting consumers from unsafe and ineffective products, considering the FDA's role in addressing information asymmetries suggests that the agency reasonably could adopt various approaches in implementing its premarket approval requirements for non-therapeutic uses.

Information asymmetries may not be as pronounced for certain non-therapeutic uses as they are for therapeutic uses. For example, people may be well-equipped to decide drugs and devices are effective for aesthetic uses.²⁷⁶ Consistent with this idea, the FDA has relied on users' own assessments as a primary indicator of effectiveness for hair growth drugs, Botox, and dermal fillers.²⁷⁷ Recreational uses of drugs or devices—if the user's goal is to have some fun—likewise may be readily evaluable by users.²⁷⁸

Yet not all non-therapeutic uses, or aspects of therapeutic uses, are amenable to user self-assessment. Unlike aesthetic and recreational uses, users may have difficulty assessing the

274. See Katz, *supra* note 249, at 13.

275. *Id.* at 8.

276. Cf. Cierra Miller, *I'm 22 Years Old & I Love Botox—Don't Judge Until You See My Photos*, STYLECASTER (Dec. 13, 2019, 5:53 PM), <https://perma.cc/DP5Y-8GRP> (providing a woman's thoughts on her Botox outcome).

277. See *supra* Part III.B.

278. Cf. *Product Reviews by Customers*, MAGIC MUSHROOMS DISPENSARY, <https://perma.cc/L5RM-DNAL> (displaying customer comments on magic mushroom and psychedelic experiences).

effectiveness of enhancing uses.²⁷⁹ As one example, some studies have suggested that Ritalin and Adderall—which are commonly believed to be effective cognitive enhancers—have only small effects on performance, and only in certain groups.²⁸⁰ Nevertheless, these drugs remain widely used for enhancement, possibly because people cannot assess drugs’ cognitive enhancing effects very well themselves.²⁸¹ Moreover, the risks of non-therapeutic uses of drugs and devices are generally similar to those of therapeutic uses.²⁸² Accordingly, even if users can evaluate benefits for themselves, users may not be able to anticipate and assess risks of non-therapeutic uses, just as patients cannot anticipate and assess the risks of therapeutic uses.²⁸³

3. Incentivizing Information Production

A third example of a purpose of the FDA’s premarket review of drug and device safety and effectiveness is incentivizing the development of societally valuable information about the products. As Rebecca Eisenberg has explained, FDA approval processes solve an information production problem by requiring manufacturers to develop rigorous evidence sufficient for the agency to assess the merits of their products.²⁸⁴ Without an FDA

279. See, e.g., Shaheen E. Lakhan & Annette Kirchgessner, *Prescription Stimulants in Individuals with and Without Attention Deficit Hyperactivity Disorder*, 2 BRAIN & BEHAV. 661, 670 (2012).

280. See *id.* at 669–70 (surveying the results of multiple studies).

281. Cf. *id.* (describing widespread use of ADHD drugs for academic performance enhancement).

282. See *supra* Part III.B.

283. Cf. *Canterbury v. Spence*, 464 F.2d 772, 781 (D.C. Cir. 1972) (“To the physician, whose training enables a self-satisfying evaluation, the answer may seem clear . . . [t]o enable the patient to chart his course understandably, some familiarity with the therapeutic alternatives and their hazards becomes essential.”).

284. Eisenberg, *The Role of the FDA in Innovation Policy*, *supra* note 21, at 370; see FDA MEMO, *supra* note 21, at 4; Kapczynski, *supra* note 21, at 2358; see also Cortez et al., *supra* note 88, at 376 (“[T]he true challenge, however, is creating a regulatory framework that encourages high-value innovation while also preventing the market from being overcome with products that are ineffective or unsafe.”).

approval requirement, drug and device manufacturers might not spend the time and money to conduct the rigorous research needed to produce this kind of information.²⁸⁵ Producing useful information about drugs and devices, in turn, helps to encourage high-value innovation—the development of new products for which there is good evidence that they do what their sellers claim.²⁸⁶ As former FDA Commissioner Margaret Hamburg said, “innovation doesn’t matter if the product doesn’t work.”²⁸⁷

Again, considering this purpose of FDA review of safety and effectiveness might suggest that there is more than one perspective on premarket approval requirements for non-therapeutic uses. On the one hand, producing rigorous scientific evidence about non-therapeutic uses may simply be less important than it is for therapeutic uses. For example, it may not a societal priority to incentivize the creation of innovative wrinkle-eliminating drugs that are superior to Botox. Notably, the FDCA carves out from the drug and device definitions—and thus the FDA’s drug and device approval standards—certain non-therapeutic uses through, for example, separately defining dietary supplements.²⁸⁸

On the other hand, incentivizing information production could be highly valuable for non-therapeutic uses. Requiring the production of rigorous information about the actual effects of novel non-therapeutic uses may necessary for realizing hopes that these technologies will be better than what has come before (or at least for understanding whether any such hopes have been realized).²⁸⁹ For instance, a highly effective and safe

285. See Kapczynski, *supra* note 21, at 2358. Retaining incentives to produce information about the effects of drugs and devices is one reason that FDA policies generally prohibit manufacturers from promoting off-label uses—if permitted to promote those uses without FDA authorization, manufacturers would lack not study them. See *id.* at 2366–67; FDA MEMO, *supra* note 21, at 11–14.

286. See, e.g., Katz, *supra* note 249, at 12.

287. Toni Clarke, *In Swansong, FDA Chief Defends Drug Approval Process*, REUTERS (Mar. 27, 2015, 8:25 PM), <https://perma.cc/4HE5-TGVY>.

288. See *supra* Part II.A.

289. Cf. Allen & Strand, *supra* note 272, at 551 (advocating for thorough vetting of non-therapeutic technologies so that society can evaluate them with accurate information about the extent of their benefits).

cognitive enhancement technology could be revolutionary in what it allows individuals, and society at large, to accomplish.²⁹⁰ Likewise, because humans have long engaged in using substances for recreation and seem unlikely to stop anytime soon, a product with a relatively safe, non-addictive, recreational use could provide a significant public health benefit. But without the scientific evidence necessary to assess the effects of such non-therapeutic uses, it would be difficult, if not impossible, to determine whether claims of enhancement or safety are supported, and challenging to predict the public health impacts of such uses.

Additionally, although the FDA is not authorized to decide social and moral questions about non-therapeutic uses,²⁹¹ scientific evidence about the safety and effectiveness of non-therapeutic uses might be necessary for individuals, or society, to answer those questions. As an example, widespread use of cognitive enhancement technologies known to have very low risks might pose different social questions than if such technologies were associated with high risks or a high level of uncertainty about their risks. Similarly, technologies that effectively, but reversibly or temporarily, enhance cognitive capabilities might raise different issues than technologies that permanently change cognitive abilities.

290. See *id.* at 550.

291. See *FDA's Response to Public Comment on the Animal Cloning Risk Assessment, Risk Management Plan, and Guidance for Industry*, U.S. FOOD & DRUG ADMIN., <https://perma.cc/T6CD-WCKG> (last updated June 11, 2020); Fox, *supra* note 36, at 1139; Gary Marchant et al., *Integrating Social and Ethical Concerns into Regulatory Decision-Making for Emerging Technologies*, 11 MINN. J.L., SCI. & TECH. 345, 347–48 (2010). Of course, the line between what is a health-related concern and what is a social or moral one can be unclear, and at times government regulators, including the FDA, have mixed social, moral, and health-related considerations. Additionally, the FDA's ultimate judgment that a use's benefits outweigh its risks (or do not) may inevitably involve social considerations. See, e.g., Lisa Heinzerling, *The FDA's Plan B Fiasco: Lessons for Administrative Law*, 102 GEO. L.J. 927, 928 (2014) (arguing that social and political considerations drove the FDA's resistance to approving emergency contraceptives over-the-counter for all ages); see also Konnoth, *supra* note 152, at 189–93 (considering the “non-health” effects of FDA-regulated drugs).

For those non-therapeutic uses that the FDA has approved, even if the FDA's ultimate approval decision may have been flawed—for example, if one disagrees with the conclusion that the benefits of Botox for facial wrinkles outweigh its risks—there is at least evidence on which to assess the risks and benefits of those uses.²⁹² The same cannot be said for non-therapeutic uses that have not been subject to premarket review requirements.²⁹³ The information production purpose of the FDCA's premarket approval provisions, thus, suggests there may be value in FDA review of non-therapeutic uses—regardless of how the FDA interprets the flexible statutory standards for safety and effectiveness.

CONCLUSION

The broadly-written drug and device definitions in the FDCA potentially subject to FDA oversight numerous non-therapeutic uses of drugs and devices, from wrinkle removers to cognitive enhancements to recreational cannabis. Although commonsense limits on the drug and device definitions are needed, this Article critiques one limit that is sometimes offered: the FDA cannot regulate non-therapeutic uses because it is impossible for those uses to meet the FDCA's safety and effectiveness standards for premarket authorization. This position will only rarely be descriptively correct, and it may not be normatively correct.²⁹⁴ The agency has been willing to conclude that the benefits of non-therapeutic uses outweigh their risks even when they are associated with small benefits, serious risks, or both—and this approach is, at least arguably, a reasonable one.²⁹⁵ Better understanding the potential scope of the FDA's jurisdiction over non-therapeutic uses, and how the FDA assesses the safety and effectiveness of such uses, is

292. See *supra* notes 187–198 and accompanying text.

293. See, e.g., Pieter A. Cohen & Scott Bass, *Injecting Safety into Supplements—Modernizing the Dietary Supplement Law*, 381 NEJM 2387 (2019) (describing safety and informational problems associated with dietary supplements).

294. See *supra* Part IV.B.

295. See *supra* Parts III.B, IV.B.

increasingly important as technological, legal, and policy developments are poised to create new markets of such uses.