PERMISSIONLESS INNOVATION IN THE HEALTHCARE SPACE: THE STORY OF 23ANDME

by Kathryn May
Abstract
Regulation, in part, determines the products that consumers can access by incentivizing or disincentivizing new innovations. The company 23andMe was forced to partially stop US sales of its genetic health testing products due to FDA regulation that was not equipped to address the modern challenges that come with exponential technological growth. This paper uses 23andMe as a case study to explore the ideas of permissionless innovation in the medical device market. A permissionless innovation approach to medical device regulation would more appropriately address the modern challenges and needs of today’s quickly changing technological landscape.

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I. Introduction

23andMe, Inc. is a California-based biotechnology company that provides direct-to-consumer ancestry and genetic testing services. The company began offering services in 2007, and it was received with public enthusiasm and excitement. It currently offers two services. Its Ancestry service ($99) gives information on an individual’s family origins. Its Health + Ancestry service ($199) gives information on inherited traits, disease risk, and carrier status for certain conditions, in addition to what is provided in the Ancestry service. In November 2013, the US Food and Drug Administration (FDA) issued a warning letter to 23andMe. The warning letter halted the company’s sales of its then-named Personal Genome Service, now the Health portion of its Health + Ancestry service. 23andMe did not begin reoffering the Personal Genome Service until October 2015, almost two years later. For a portion of the time that Personal Genome Service sales were shut down by the FDA, 23andMe provided its full product line to select markets outside of the US. 23andMe launched its Personal Genome Service in Canada and the United Kingdom about a year after its US operations were put on hold.

The Health service results that 23andMe offered in 2015 were pared down significantly compared to 2013 results. In 2013, the company offered risk assessments for 254 diseases and conditions.1 The 2015 relaunch of the Health service included only reports that were explicitly approved by the FDA. The new reports were limited to carrier status reports for 36 diseases and wellness reports for traits like lactose intolerance and alcohol flush. In spite of the decreased offerings, the price had doubled from $99 for the Personal Genome Service to $199 for the

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This paper uses 23andMe as a case study to explore the ideas of permissionless innovation in the medical device market.

II. Background

23andMe is a biotechnology company that provides genetic and genomic testing. It was founded by Anne Wojcicki, Linda Avey, and Paul Cusenza in 2006, with the mission to “help people access, understand and benefit from the human genome.” In 2007, 23andMe began offering its Personal Genome Service® and became one of the first direct-to-consumer genetic testing companies. The company uses “data to revolutionize health, wellness, and research.” In 2008, its human genomic testing was named Time magazine’s Invention of the Year. Today, the company offers two services: genetic ancestry-only testing and combined genetic ancestry and genomic health testing.

The company’s claim to fame is its at-home testing kits. The first service 23andMe offered tests a customer’s DNA for ancestry composition, maternal and paternal haplogroups (genetic groups that show common ancestry), Neanderthal ancestry, and DNA family. At its

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3 Genomics is the study of an organism’s genes. All 23,000 genes together are called the genome. Genetics, on the other hand, is the study of heredity.
5 Ibid.
launch in November 2007, the Personal Genome Service, then just an ancestry report, cost consumers $999.\textsuperscript{10} The following December, the price was reduced to $399. On April 23, 2010, 23andMe tested a one-day price drop to $99 in celebration of DNA Day. It sold out. Today, 23andMe offers its now-named Ancestry Service for $99 and its new Health + Ancestry Service for $199. The Health + Ancestry Service tests for genetic health risks, wellness, genetic carrier status, and genetic traits, as well as everything included in the original Ancestry Service.\textsuperscript{11}

One of the factors that makes 23andMe popular is its easy access. Once a customer places an order, a testing kit is mailed and arrives at her home in 3 to 5 days.\textsuperscript{12} The kit includes a collection tube, which the customer fills with her saliva. The filled tube is registered to the customer with a barcode. The kit is then returned to the company, and results are provided to the customer in about 6 to 8 weeks. Results can be accessed and interacted with online. Customers also have the option of purchasing kits at third-party retailers, such as CVS, Walmart, and Amazon.\textsuperscript{13} 23andMe started as a highly innovative and promising company, but encountered regulatory roadblocks and eventually halted sales of one of its products after receiving a warning letter from the FDA.

\textbf{23andMe and the FDA}

23andMe is classified by the FDA as a medical device under section 201(h) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 321(h). Section 201(h) specifies that

“The term “device”… means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is—

(1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
(2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
(3) intended to affect the structure or any function of the body of man or other animals, and
which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term “device” does not include software functions excluded pursuant to section 360j(o) of this title.”

There are three classes of medical devices under FDA regulations. Class I and II devices are considered to have a low risk of harm to patients and typically do not require clinical trials. Class III devices are considered to have a higher risk of harm to patients and require premarket approval from the FDA to ensure safety and efficacy. Any new device that does not fit into an existing category (i.e., is novel) is automatically considered a Class III device, regardless of risk potential. Because the Personal Genome Service did not fit into an existing category, 23andMe’s Personal Genome Service is considered a Class III medical device.

23andMe has had a tumultuous relationship with the FDA. The first public interaction between 23andMe and the FDA was in July 2012, six years after the company was founded.
23andMe posted a press release stating it was making the first steps toward FDA clearance.\(^1\) In November 2013, 23andMe received a warning letter from the FDA.\(^2\) The FDA had sent the company four other letters on the topic of regulatory issues with the Personal Genome Service over the preceding 14 months without receiving a satisfactory response. Although 23andMe had attempted to stress that the results of their genetic tests were not medical diagnoses, the FDA letter claimed that marketing 23andMe’s Saliva Collection Kit and Personal Genome Service without FDA approval was in violation of section 201(h) of the Federal Food, Drug, and Cosmetic Act. The FDA alleged that 23andMe had not “analytically or clinically validated the [Personal Genome Service] for its intended uses.” 23andMe was ordered to halt sales of its health-related genetic tests, or the “Health” portion of the Health + Ancestry tests, until the company had completed FDA regulatory review.

23andMe received a follow-up letter from the FDA on March 25, 2014 stating that the company had adequately addressed the violations of the 2013 warning letter.\(^3\) In February 2015, FDA issued guidance that allowed for alternate pathways to clearance when a device is considered novel.\(^4\) Following this announcement, 23andMe announced it would follow this pathway for its direct-to-consumer genetic tests.\(^5\) From receipt of the initial warning letter until

October 2015, 23andMe offered only ancestry reports and raw health data to customers. Customers could download their raw data and input it into a third-party genetic analysis service to have their genetic data interpreted, but 23andMe could not offer genetic data interpretation during that time. This pathway allowed 23andMe to bring back more than 35 carrier status reports that convey inherited risk of developing a disease or condition.

The 2014 FDA interaction was not 23andMe’s first run-in with the bureaucracy. In late 2007 and early 2008, New York State’s Department of Health sent warning letters to 23andMe and a number of other genetic testing companies. In June 2008, the company and 13 other genetic testing companies received a cease-and-desist letter from the California Department of Health. In August of the same year, 23andMe received a California license to offer its direct-to-consumer services. According to a 2007 survey by Johns Hopkins University’s Genetics and Public Policy Center, only 26 states allowed direct-to-consumer testing. An additional 12 states offered “limited” direct-to-consumer testing. New York offered testing only through a licensed physician, and California allowed direct-to-consumer testing only of “pregnancy, glucose level, cholesterol, occult blood” and certain FDA-approved over-the-counter tests. This paper will focus on federal, rather than state-level, government interactions and regulations.

**De Novo Pathway**

The Food and Drug Administration Modernization Act of 1997 established the *de novo* pathway by adding Section 513(f) (2) to the Federal Food Drug and Cosmetic Act.\(^{29}\) The *de novo* pathway gives the FDA the ability to classify new medical devices that do not fall into a preexisting category – which would otherwise automatically be classified as a Class III device and require premarket approval – as Class I or Class II devices that require a risk-based evaluation by FDA but do not require premarket approval.\(^{30}\) This mechanism has allowed 23andMe to offer over 40 carrier status reports that convey the potential of passing a gene to offspring, nine genetic health risk reports, and a cancer risk report directly to consumers.\(^{31}\) Because the pathway is available only for new devices, it cannot be used for 23andMe’s products that had already been deemed as needing premarket approval, including the Personal Genome Service.

23andMe launched its health risk reports after receiving clearance through a *de novo* pathway. In April 2017, 23andMe began offering direct-to-consumer genetic health risk information.\(^{32}\) In contrast to the already approved carrier status reports that convey inherited risk, these genetic health risk reports convey personal health risk. Therefore, they required a separate *de novo* pathway. The *de novo* clearance was specifically for reports on personal risk for developing ten genetically linked conditions, including Parkinson’s disease and Celiac Disease. The clearance also created a pathway for future, substantially equivalent reports to receive a...

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\(^{30}\) Initially, the requirement to request a risk-based classification came only after submitting a 510(k) submission, but, in 2012, this requirement was dropped so that companies could directly request a risk-based classification.


class II exemption from the FDA, streamlining the process of making reports available to consumers.

Through a third *de novo* pathway, 23andMe began offering direct-to-consumer cancer risk reports in March 2018. These reports are the first cancer risk reports offered to consumers without a prescription or without needing the request of a doctor. They provide risk information on three genetic variants associated with heightened risk for breast, ovarian, and prostate cancers. According to 23andMe, these variants are most common in individuals of Ashkenazi Jewish descent, and about 1 in 40 individuals (about 2.5 percent) of Ashkenazi Jewish descent will have one of the three genetic variants. Women displaying one of these genetic variations “have a 45-85 percent chance of developing breast cancer by age 70.”

**III. Permissionless Innovation**

For 14 months, 23andMe ignored an FDA letter warning that the company was not compliant with FDA medical device regulations. A 14-month period of silence is considered by the FDA to be enough reason for the agency to shut down any company. This is evidenced by the production shutdown of the medical device company Accurate Set, Inc., mandated by the FDA after only five months of nonresponse.

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34 Ibid.

Some praised the FDA’s decision to halt 23andMe marketing of its genetic health testing services as necessary for reasons outside of their non-response. Since 23andMe markets directly to consumers, many experts worried about the ramifications of inaccurate results. Individuals could act on the results without medical professionals giving context to test results or acting as intermediaries. Experts cited lack of data on how consumers might change their behavior based on test results, especially because 23andMe was the first direct-to-consumer genetic test. No company had yet proven that an average consumer could properly interpret and react to the data they received. The 23andMe warning letter pointed out the risk that “patients relying on such tests may begin to self-manage their treatments through dose changes or even abandon certain therapies depending on the outcome of the assessment.”

This type of outlook is an example of the precautionary principle in practice. The precautionary principle states that public policy should protect against potential harms, especially irreversible harms, even if those harms exist only in theory and potentially would not exist in reality. The precautionary principle puts the burden of proof on the innovators in order to prove a product’s safety and efficacy before that product can be marketed. In the case of 23andMe, the precautionary principle required the innovator prove a product would not be misused or misinterpreted by consumers. Proponents of the precautionary principle are willing to sacrifice potential innovations for increased safety or an increased perception of safety. Government

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regulations of new technologies intend to prevent harm, but without adequate risk information, they trade one risk for another. Those technologies that are prevented by regulations could have become the cancer cure or the vaccine or the reusable carbon neutral rocket ship of the future. Without allowing these technologies to come to fruition, we cannot know their true potential or value.

Permissionless innovation stands in opposition to the precautionary principle. Permissionless innovation posits that “technological progress requires above all tolerance toward the unfamiliar and the eccentric.” Adam Thierer argues that permissionless innovation is akin to freedom, claiming that “there is a symbiotic relationship between freedom and progress.” Proponents of permissionless innovation do not deny that some innovations will fail. They argue that, “We need to keep trying and even failing in order to learn how we can move forward.” It is necessary to have both beneficial and useless innovations in order to create a dynamic churn of ideas and, thus, progress.

Global innovation arbitrage is the movement of innovation from one part of the world to another with less onerous regulations. It is also a way that companies can punish regulatory environments that are too precautionary and burdensome. Global innovation arbitrage is the relocation of innovation and innovators to “those countries and continents that provide a legal and regulatory environment more hospitable to entrepreneurial activity.” In this manner,

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countries with burdensome regulatory environments can benefit from global innovation arbitrage by allowing risky new technologies to be field-tested across the globe before they are introduced into domestic markets. The loss to a country with excess regulatory burdens would come from production job, forgone GDP, and the lack of innovative health technology.

An example of global innovation arbitrage in practice is the nonmilitary drone market. In 2014 and 2015, the Federal Aviation Administration (FAA) was preparing to produce new regulations on the drone market. Safety was a primary concern, but those who saw the potential benefits of the technology, rather than solely the risks, advocated for looser regulation to allow for greater future innovation. At the time, technology columnist and author Farhaad Manjoo wrote, “Federal drone restrictions have a single purpose in mind: safety…. If the F.A.A.’s draft rules come in as expected, they would cut out a wide range of faraway uses, including agricultural applications like overhead crop monitoring or industry uses like the inspection of oil pipelines or electrical lines from afar.”

During the public comment period, Amazon wrote in a letter to the FAA: “Without the ability to test outdoors in the United States soon, we will have no choice but to divert even more of our UAS [Unmanned Aerial Systems] research and development resources abroad.” The threat of such a large company taking research and development money out of the country and putting it into a foreign economy was not enough to allow Amazon to get permission to use drones for US deliveries.

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When 23andMe was partially shut down by the FDA, it was still allowed to continue marketing its full product line outside of the US. 23andMe launched its Personal Genome Service in Canada and the United Kingdom about a year after its US operations were put on hold.45 Customers’ kits were still sent to the US for testing.46 The company could therefore continue to generate revenue for its genomic health testing even though its original market was on ice. In April 2015, six months before it received FDA approval to renew marketing of Health testing, 23andMe added Denmark, Finland, Ireland, the Netherlands, and Sweden to its international sales.47

Risk Tradeoffs and Regulation of New Technology

Regulation, at its core, is intended to mitigate risk and improve safety. All new ideas and technologies come with inherent risks, no matter how harmless they seem, or how vast their potential to create good may be.48 For example, pesticides allow our farmers to greatly increase their yields and thereby reduce food insecurity, but they also put the animals and humans that eat them at a marginally heightened risk for certain illnesses, including cancer.49 Regulating pesticides used on fruits and vegetables increases the price of the produce and may inadvertently cause consumers to eat foods that are less healthy.50 Risk-risk tradeoffs such as the one are

important and impactful for wellbeing, but are all too often ignored. Frequently, regulatory authorities dismiss benefits that can be provided when new risks are introduced by a new technology.

Incorrectly valuing risks or benefits can lead to poor allocation of resources. As Aaron Wildavsky points out, “richer is safer.” Expenditures on risk mitigation increase safety only so long as the benefits outweigh the costs. Societies and governments should attempt to use money and brainpower efficiently by allocating those resources to mitigate the most risk at the least cost. In reality, cost is often ignored as regulation is used to push risk toward zero. In the late 1960’s, after the home pregnancy test was ideated but before it was brought to market, it was feared that women would not be able to handle receiving the results of a pregnancy test without the presence of a medical professional. Some doubters of the home pregnancy test worried that a hysterical teenager might “[jump] off a bridge” after finding she was pregnant out of wedlock, and feared that women “in a state of emotional anxiety” would be unable to follow “the simplest instructions” when self-administering the test. Therefore, many experts believed that pregnancy tests should be offered only by doctors in doctors’ offices, regardless of the excess strain this put on doctors’ time. In trying to mitigate risk, they ignored or discounted possible cost-savings. We now know home pregnancy tests as a modern convenience that allow women and couples to take more ownership of their health and family planning. In spite of the fears perceived by many, home pregnancy tests have been successfully and safely used by vast amounts of consumers, and have freed up doctors’ time for other valuable uses.

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The actual allocation of resources for risk mitigation is heavily dependent on risk perception rather than reality. As Epstein observed, “in everyday life that people apprehend reality in two fundamentally different ways, one variously labeled intuitive, automatic, natural, non-verbal, narrative, and experiential, and the other analytical, deliberative, verbal, and rational.” It follows that there exist multiple categories of risk-benefit perception and weighting as well, with each based on groups’ perceptions of risks. In fact, it’s been shown that different groups perceive risks in differing ways. The general public has been found to be polarized on the perceived risks of pesticides and genetically modified foods. Individuals in Hungary, a poorer and less advanced nation than the US, perceive risks at much lower levels than individuals in the US, in spite of the fact that the two groups rated the risks with similar qualities such as catastrophic potential. Americans assigned higher perceived risks to new technologies and lower risks to everyday hazards relative to Hungarians.

In a world where it is impossible to forgo risk entirely, good regulation promote trial-and-error risk taking. Aaron Wildavsky wrote: “trial-and-error risk taking, rather than risk aversion, is the preferable strategy for securing safety. Encouraging trial and error promotes resilience — learning from adversity how to do better — while avoiding restrictions that encourage the continuation of existing hazards.”

### IV. 23andMe and Innovation

23andMe entered the marketplace as one of the very first direct-to-consumer genetic testing companies in the world. With that, it had the opportunity to disrupt existing markets and hierarchies by democratizing the way that consumers accessed their genetic data.

Much of the value that 23andMe has created can be seen in the company’s lengthy list of publications. The company built the world’s largest interactive genetic research platform by crowdsourcing data from its Personal Genome Service customers. By tapping into the existing, assessable data of its millions of customers, 23andMe has created an unprecedented amount of data that can be used for health and genetic research. 23andMe states that it has genotyped more than 3 million customers, with over 85 percent of its customers opting to participate in research. The company has a more than 2.5 million genome database from which it can find trends and health linkages.

This has proven to be a powerful research tool. Customers have the option to opt-in to participation in research, and those who have opted-in have contributed to over 230 studies on a variety of topics. The company itself has produced 94 “peer-reviewed, published genetic studies on disease and wellness, including studies on genetic associations for melanoma, schizophrenia, cognitive empathy, and endometriosis, among others.” 23andMe published its first study using data collected through its genome testing services in 2010. Haydeh Payami, of

the New York Department of Health, stated, "[what] 23andMe did in a matter of years would have taken several decades and tens of millions of dollars if done conventionally." 61

Investors have responded to 23andMe’s historic and current potential for value creation. In September 2017, 23andMe received $250 million in growth financing. 62 Before that, the company had most recently conducted financing during its Series E round in October 2015. This Series E round, which occurred only months after the company announced the new FDA regulatory pathway for its direct-to-consumer tests, raised $115 million. 63 In total, 23andMe has raised $491 million in financing since the company’s birth in 2006. 64 23andMe is now valued at roughly $1.5 billion. 65

Impact on Innovation and Access

23andMe was a first-of-its-kind company when it hit the market. Naturally, competitors quickly came to jockey for space in the wide-open direct-to-consumer genetic testing market. There were four major players in the consumer-facing genetic health testing market at the time that 23andMe was issued its FDA warning letter: 23andMe, deCODE, Navigenics, and Pathway Genomics. 66

Icelandic company deCODE brought its product deCODEme to the U.S. market in November 2007, several months after the Personal Genome Service became available. Its introductory price of $985 slightly undercut the 23andMe price of $999 at the time. DeCODEme was a very similar product to 23andMe’s Personal Genome Service. DeCODEme offered information on ancestry, “obvious and potentially quirky traits,” and risk potential for some common diseases, as well as an online interface.\(^\text{67}\) DeCODE stopped offering its deCODEme service in 2014, about a year after 23andMe received its FDA warning letter. DeCODE stopped offering its online interface for existing deCODEme customers on January 1, 2015.\(^\text{68}\)

Navigenics was a personal genomics company based in California. The company launched in November 2007, the same month the deCODEme service entered the market.\(^\text{69}\) Navigenics began selling its genetic testing service Health Compass in April 2008. Navigenics offers its service through physicians only, rather than directly to consumers. At the time of its launch, Health Compass (a Navigenics product) gave “individuals information on their chances of developing up to 18 common conditions, so that with their physicians, they [could] obtain earlier diagnosis, delay onset or prevent the conditions altogether.”\(^\text{70}\) It is unclear what the original price of the service was, but it was lowered to $999 in July 2009.\(^\text{71}\) Navigenics was


acquired by Life Technologies in 2012.72 Life Technologies was in turn acquired by Thermo Fisher Scientific in 2014,73 before Life Technology’s product offering was merged into Thermo Fisher Scientific’s other brands.74 Thermo Fisher Scientific’s Applied Biosystems brand offers genetic analysis to laboratories and researchers for research purposes. It does not offer a service similar to the Personal Genome Service for general consumers.75 Notably, Navigenics shared 23andMe’s state-level regulatory issues. Both New York and California sent Navigenics formal letters threatening or halting its service at the same time that letters were sent to 23andMe. Navigenics also received a license to do business in California at the same time as 23andMe.

Pathway Genomics, also based in California, was founded in 2009. The company offers “physician-ordered tests [that] include assays for diet and weight loss, circulating tumor DNA mutations (liquid biopsy), hereditary cancer and carrier screening, as well as metabolic response for many commonly prescribed medications” as well as a non-invasive cancer test.76 The company planned to offer an IBM Watson-powered mobile app to give personalized health and wellness recommendations. The company has followed its vision of making “comprehensive genetic testing and personalized medicine accessible and affordable to all” by pursuing medically oriented testing.77 This stands in contrast to 23andMe’s educationally-focused testing.

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Of the four main players in the personal genetics testing market at the time 23andMe received its warning letter, only 23andMe and Pathway Genomics continue to offer substantively similar tests. DeCODE eliminated its testing service. Navigenics no longer exists, with its consumer-facing genetic testing service lost during the former company’s second acquisition. Pathway Genomics has been successful, but it does not offer a direct-to-consumer test. Thus, 23andMe is the lone survivor of the early days of personal genetic testing that offers easy access to consumers. Market churn is normal and healthy, but it would be difficult to argue that government regulation did not contribute to the outcomes of the early actors in this market. It is also likely that it dissuaded potential firms from entering the market after watching 23andMe lose an enormous amount of potential revenue and investment opportunity. Particularly in the case of Pathway Genomics, which has successfully navigated regulatory red tape for almost a decade, there is little incentive to rebrand as a direct-to-consumer firm. Pathway Genomics lacks brand recognition in the direct-to-consumer market, and direct-to-consumer offerings require additional regulatory burden and the costs and risks that accompany it. The US is currently without a competitive, multiplayer market for direct-to-consumer genetic health testing.

Not only did the FDA regulatory burden and enforcement scare off existing firms, but it also left a vacuum in that space for illegitimate companies to fill. A simple Google search for any variation of “genetic health test” yields more than a handful of companies seeking your business. Most of these companies appear to be foreign-owned companies and offer little information about their validity. Whether they are legitimate or not, they almost certainly do not meet the precautionary standards that the FDA sets to protect US consumers. The internet has made it nearly impossible to prohibit an individual with a strong desire for information from finding a source for it. Inadvertently, the FDA’s strict regulatory structure shut out legitimate, if untested,
businesses and left unsubstantiated online portals as the most prominent direct-to-consumer option available. The FDA thwarted its own intention of protecting consumers from untested companies by making unapproved, unregulated companies some of the easiest options for consumers.

The story here isn’t what happened to 23andMe or any of its competitors individually; it’s about what happened in the market as a whole. The FDA warning letter that halted 23andMe’s Health services directly or indirectly produced a market with severely limited options for consumers. Yes, consumers could still get their genetic data tested through a physician. Yes, consumers could input already-sequenced data into an online processor that would offer outputs similar to what 23andMe had offered. The nuance here is the marginal effect of this added bit of effort required for a consumer to access his genetic data. Any bit of additional friction will cause some consumers to decide the effort isn’t worth it. The greater the friction, the greater the quantity of consumers who drop out.

Because 23andMe and its original competitors are private companies, they do not share metrics such as sales data. Thus, it cannot be known with certainty how impactful the FDA warning letter was on consumer choice. In spite of this limitation, there are market signs that we can look at to get an idea of the impact. Three years after 23andMe received regulatory clearance for its health tests, there has not been a significant competitor that has come into the genetic health testing space to challenge 23andMe. Given how much money Americans are willing to spend on ancestral DNA testing (almost $100 million in 201578) to increase their genetic knowledge or services such as gut biome tests (expected market cap over $500 million by

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or boutique gym memberships (over $9 billion in 2016) in order to improve their health, the demand for direct-to-consumer genetic health tests is certainly greater than $0. In spite of this, the regulatory environment has restricted access to direct-to-consumer genetic health tests for a number of years.

Consumer choice is not the only loss to stem from the market changes that occurred. Consider the almost two years during which 23andMe’s Health services were not offered. During that time, fewer people purchased 23andMe’s genetic testing than would have if the Health services had been offered. Many scientific articles use 23andMe’s genetic database to find trends and linkages in genetics and health outcomes. With fewer people in this database, those studies are less robust. It is possible that life- or quality-of-life-saving findings were either delayed or have not yet been discovered due to the smaller database. The smaller genetic database is particularly harmful to ethnic minorities and individuals with rare conditions. Most genome-wide association studies rely heavily on genomes of individuals of European decent. Less genomic data collection also means less genomic data diversity and fewer genetic association findings that are relevant to individuals not solely of European decent. The same is true for individuals with rare conditions. Less new genomic data means less data to learn what causes and prevents those rare conditions.

Bernard Munos, Senior Fellow at The Milken Institute’s FasterCures and honoree in FiercePharma’s 2012 Top 25 Most Influential People in BioPharma,\(^8\) described the ramifications of the FDA warning letter best. In an opinion piece published just a week after the FDA warning letter was published, he wrote:

“FDA acted properly in view of 23andMe's cavalier attitude toward its regulatory obligations and its failure to meet past commitments. However, it would be a setback for science if 23andMe were not allowed to proceed. For its research model to deliver, it needs more people, far more people in its database. A campaign to sign up a million customers is a good start, and not losing momentum is essential…

This spat is bigger than 23andMe. It's about another way to do science that can greatly enrich the current dominant approach that is based on the 65-year old randomized-controlled trial concept. We all stand to gain if 23andMe -- or its eventual licensee -- succeeds. Let's give it a chance, but be clear about the consequences.”\(^3\)

As Munos pointed out, the FDA was right to punish 23andMe for the company’s noncooperation. The righteousness of the punishment is separate from the harm that came from the punishment. 23andMe was foolish to ignore the FDA, and under current law, the FDA was justified to react as it did; however, consumers lost out in the end.

**23andMe and Global Innovation Arbitrage**

Global innovation arbitrage, as discussed above, is a method by which companies can punish burdensome regulatory environments by taking their business to other countries. 23andMe engaged in global innovation arbitrage during the period in which its genetic health reports were shut down in the US by the FDA. The company already sold its ancestry service in other countries, but it sought to find a good business environment for its health reports after they were

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halted in the US. It was reported that 23andMe was looking to move its Health reports into other English-speaking markets by the end of 2014.\textsuperscript{84} The company expanded the full service into Canada and the UK a year after its receipt of the FDA warning letter.

23andMe currently offers its full Health + Ancestry service in the U.S., Canada, the U.K., and select E.U. countries (Finland, Ireland, Netherlands, Denmark, and Sweden). Other international markets are able to buy only Ancestry reports. Customers in countries where the Health service is not offered can still opt-in to have their genetic data used for research studies including ancestry, traits, and disease.\textsuperscript{85}

23andMe’s international sales allowed it to innovate more actively in its Health testing than it would have been had its health testing capabilities been completely on hold. Again, 23andMe does not offer metrics that allow us to determine exactly how successful its Health testing has been overseas and north of the border. It is almost certain, though, that the company continuing to provide its Health service, even in a decreased capacity, allowed it to improve and refine its product during the time that it was halted in the U.S.

The international markets that had access to 23andMe’s Health testing did not endure any of the adverse effects that were feared by American experts and regulators. Customers were able to appropriately handle information on their genetic health risks without the presence or guidance of a trained professional. The possibly disqualifying risks of allowing common people increased access to their genetic health information seem to be similar to the risks of giving women and couples increased access to their pregnancy status: perceived yet not realized. In


some ways, this is good news for America. The US was able to defer taking on a possibly risky product until the product had been tested and proven safe in other markets. American markets gained by effectively mitigating risk, but also lost out on the gains that come from early adoption of the new technology. American citizens and residents were unable to conveniently access their genetic health data. 23andMe was also incentivized to more actively pursue other markets and as it lost a main product in domestic markets. Fewer Americans’ genetic information was added to 23andMe’s database and available for utilization in scientific studies. Finally, the US lost out on the additional jobs and GDP gains that could have come from domestic purchases of 23andMe’s health tests. The US was able to mitigate the perceived risks of 23andMe’s health tests, but it was forced to realize some very real costs in return.

V. Policy Implications

It’s clear that the 23andMe and FDA legal disputes caused an outcome that was imperfect. In addition to the obvious revenue loss from banned sales and bad publicity, 23andMe lost out on a valuable opportunity for innovation. Instead of having the most groundbreaking portion of its product offering on ice for several years, the company could have increased its product offering and increased the diversity and size of its database, possibly leading to scientific breakthroughs that were at best pushed back a few months or years or prevented entirely. The threat of legal action that loomed over competitors pushed them away from the market space that 23andMe once held. This left consumers with significantly decreased options, whether they were looking to take more control over their personal health or simply expand their knowledge of their own health. Consumers who may have been made better off by the health breakthroughs caused by a better understanding of genetics and genetic interactions with modern healthcare were unable to
realize those potential health benefits. By shutting down 23andMe’s Health services, the FDA likely decreased innovation and caused losses to health, wealth, and wisdom.

FDA was put in an impossible position by 23andMe. It remains unknown what the agency’s intention was during its preliminary dealings with 23andMe, but it is plausible based on early interactions between the two that the FDA was holding off on regulatory enforcement while 23andMe was actively seeking out regulatory approval. Regardless of whether the FDA planned to bring regulatory enforcement measures against the company, 23andMe is at fault for being unresponsive to a regulatory warning letter. Companies are typically expected to address the factors that caused the warning letter within a time frame that the company and the FDA agree upon together; however 23andMe did not respond to create a timeline to address the Agency’s concerns. Regardless of its original intent, the FDA would have set a visible precedent of allowing noncompliant companies to ignore its mandates and communications if it had not brought legal action against 23andMe.

Regardless of the errors of 23andMe, the FDA is tasked with its congressionally mandated mission that includes “protecting the public health by ensuring the safety, efficacy, and security” of health products, food, and cosmetics.86 Its regulations must be enforced. For many companies, now and in the future, the structure of those regulations is not dynamic enough to get new and innovative products to market in a timely manner. The FDA reconcile its duties of ensuring safety and enforcing existing regulations with the reality that many of these regulations are outdated or ill-suited for modern products.

FDA would be best advised to take inspiration from the idea of Hidden Law. As described by Brookings Institute Senior Fellow Jonathan Rauch, Hidden Law is “the norms,

conventions, implicit bargains, and folk wisdoms that organize social expectations, regulate
everyday behavior, and manage interpersonal conflicts." 87 More simply, Hidden Law comprises
those unstated agreements we make in order to make social living easier and more comfortable.
Rauch gives the example of how society handles adultery as an illustration of Hidden Law at
work. In his example, we tell our kids that infidelity is absolutely never allowed, yet in reality,
society tolerates some amount of adultery— with the caveat that it must be covert. This gives
cuckolded partners the option of handling the affair as they see fit, whether it is by ignoring it,
working out some sort of arrangement, or otherwise addressing it internally to the marriage in
order to save the marriage and save face. It also gives the cuckolded partner the option of outing
the cheater to the rest of society, at which point he or she will be shamed and ostracized. 88 This
unspoken arrangement society has created gives partners control over how to handle extramarital
affairs while allowing society as a whole to agree that those affairs are shameful and to use the
threat of public shaming to deter couples from violating societal norms.

As a federal agency, FDA’s authority and mandate come from Congress. There are
certain laws that the agency must follow with little wiggle room for interpretation or for restraint.
Not all laws that FDA implements, however, are so tightly constraining. In some cases, FDA
does have an opportunity to allow flexibility for innovation through its rulemaking process.
Finalized rules, set by the agency instead of Congress, can be repealed or altered through the
same process through which they were enacted, as outlined in the Administrative Procedures Act
mentioned above. This process may be lengthy, but it will allow the FDA to remove or loosen

87 Jonathan Rauch, "Conventional Wisdom: Rediscovering the Social Norms That Stand between Law
and Libertinism," Reason, February 2000, accessed May 14, 2018,
https://www.jonathanrauch.com/jrauch_articles/hidden_law_2_why_i_am_communitarian/.
88 Jonathan Rauch, "Law and Disorder: Why Too Much Due Process Is a Dangerous Thing," The New
Republic, April 30, 2001, accessed April 14, 2018,
http://www.jonathanrauch.com/jrauch_articles/hidden_law_1_the_legal_assault/.
overly burdensome rules. In addition, Congress pays particular attention when the agency sees
the need for more flexibility and can change laws accordingly. The agency can also adopt a less
stringent interpretation of the finalized rules in order to allow for more flexibility.89

**Soft Law**

Soft law presents a useful framework for the FDA. The term soft law refers to “quasi-legal
instruments that have no legal force, such as non-binding resolutions, declarations, and
guidelines created by governments and private organizations.”90 The use of soft law has gained
popularity since the concept first emerged in international law in the 1980s. Since its inception,
soft law has become increasingly relevant in America’s domestic legal culture, especially as
regulators and lawmakers struggle to keep pace with technological change and innovation.

Soft law has been particularly useful for international agreements. It facilitates regulatory
cooperation between countries without sacrificing autonomy and sovereignty. Global, systemic
issues such as environmental or bioethical concerns are especially well suited for international
soft law agreements. The agreements are substantive and harmonize the participating countries’
legal expectations; however, they are not directly enforceable in the same manner as hard law
treaties and statutes.91

In the same way that soft law can be effective at harmonizing international groups’
expectations, it can also be effective domestically. Domestic soft law can be particularly

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effective in sectors experimenting with new technologies and business practices. Soft law can address the ‘pacing problem,’ which is the lag between a new technology’s introduction and the development of legal measures to control that technology and ensure safety. The pacing problem is exacerbated by the fact that new technologies are being adopted more quickly after their introduction to markets. Because soft law can be shaped to fit each unique situation, it is flexible enough to bridge the gap between modern expectations, outdated legal frameworks, and new innovations.

The Administrative Procedure Act requires all rulemaking to include a notice and comment period before the rules are promulgated. These rules are considered legislative rules. Non-legislative rules, which are not meant to have a binding legal effect, are generally exempt. Circulars, advisories, and some guidance issued by agencies are considered non-legislative rules, and are good examples of soft law in practice. Sometimes, it can be hard to differentiate between legislative and non-legislative rules. However, questions about the type of rule can be sorted out in court. In general, courts have found that non-legislative rules are considered “interpretive rules” or “general statements of policy.”

It is worth noting that soft law has the potential to turn into hard law, or legally binding law. This feature of soft law makes it an attractive option for governing new or rapidly changing

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sectors. A regulatory body can effectively launch a trial run of a legal framework using soft law. Because soft law is more agile than hard law, any aspects of the soft regulatory framework that are identified as overly burdensome or that don’t offer enough consumer protection can be addressed quickly. When a successful regulatory framework is eventually found through a process of trial and error, that framework can be, although in many cases need not be, codified into hard law.

Soft law is often better suited than hard law to creating a resilient regulatory environment. In the modern world of exponential technological growth, our regulatory environment should be agile and mutable in order to address the quickly changing risk environment. As the sources of potential risk grow and become increasingly complex, traditional hard law risk management techniques suited to fixed, straightforward and predictable risks become less appropriate. A resilient regulatory environment that seeks “to minimize the severity or duration of unanticipated harm once an adverse event or outcome has occurred” will be most effective.98

Government regulations of new technologies with the intention of preventing harm to individuals and society come with a very real risk-risk tradeoff: those technologies that are prevented by regulation could have become life-improving innovations. Without allowing these technologies to come to fruition, their true potential or value cannot be known.

**Soft Law in Practice**

By using soft law guidance where it is permissible by law, the FDA can choose to take legal action against only those companies that cause actual harm or are have actual, rather than

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perceived or theoretical, potential to cause irreversible and terrible harm. Just as with the case of Hidden Law for adulterers, this gives power to consumers to interact with health companies and providers as they wish without outside interference, but leaves open the option to “throw the book at” firms that violate the explicit expectation to not cause real harm. This solution also follows Thierer’s notion of regulating only those situations in which harm is highly probable, tangible (physical), immediate, irreversible, or catastrophic.99 Unlike in the case of unspoken Hidden Law, the FDA can state unambiguously its intention of enforcing regulation in this manner. This gives firms the confidence to innovate and quickly move products and ideas to market without fear of government interference and maintains the authority of the FDA to step in should a company truly endanger consumers. With this solution, both the FDA and companies will have explicit guidelines suitable for regulating a quickly changing technological landscape.

The FDA has already begun to utilize soft law. In November 2017, FDA Commissioner Dr. Scott Gottlieb, MD issued a statement declaring that the FDA is reevaluating how it regulates direct-to-consumer genetic health tests.100 Commissioner Gottlieb stated the FDA is “creating pathways that are risk-based, efficient, achieve the assurance of safety and efficacy, and in the case of tests, analytical and clinical validity, through a framework that is least burdensome.” In doing so, the FDA has already built flexibility into some of its new programs. In the case of genetic health tests, FDA is exempting the tests from premarket review as long as the tests meet certain outlined criteria, and it will allow all tests from a given company to enter the marketplace so long as the first test the company introduces is reviewed by the FDA. Other parts of the wider

99 Adam Thierer, Permissionless Innovation: the Continuing Case for Comprehensive Technological Freedom (Arlington: Mercatus Center at George Mason University, 2016), page 34.
medical device market that have seen FDA soft law guidance include in vitro diagnostic devices, HIV treatment development, asthma inhaler quality standards, laser products, and statistical principles for clinical trials, among others.\textsuperscript{101}

These modern, more flexible legal expectations for companies will allow increased consumer choice in markets and will allow new innovations to enter the market more quickly. This type of flexible regulatory structure will be more robust as future technologies and innovations test its efficacy. As the FDA institutes more flexible regulatory oversight in genetic health testing markets, it should also seek more flexibility in all of its markets. Protecting consumers from tangible and catastrophic harm remains a paramount duty of the agency. However, as technology continues to progress and be adopted at an increasingly rapid pace, stalling a technology unnecessarily due to outdated regulatory mechanisms will often do more harm than good. In the event that consumer harm occurs, consumers can use our existing common law and file a civil suit against companies. Civil courts under our current regulatory regime serve to deter bad actors and to compensate injured parties.

Increased flexibility also allows resources to flow to where they are most useful.\textsuperscript{102} By focusing on flexibility, the FDA can avoid expending large amounts of resources on circumstances unlikely to cause harm, such as by conducting very thorough reviews of new tests very similar to existing, already approved tests. Instead, the agency can use those resources to punish wrongdoers who have inflicted real harm or who have clearly disregarded the established safety standards. Leaving behind rigid, antiquated rules will require deftness from the FDA


\textsuperscript{102} One example of where FDA has done this in the past is food standards. In first several decades after the 1938 act that required them, FDA invested a great deal of resources in establishing them. However, in the past several decades, funding for food standards is been extremely low.
leadership. Rather than relying on clunky protocol, the FDA will be forced to weigh risk tradeoffs and ration their resources with situational awareness. Ultimately, the FDA will be rewarded for the effort by being much closer to their mission to protect the public health, because it can continue to prevent harm while also allowing the vast potential benefits of new innovations to increase health, wealth, and quality of life.

**Consumer Risk Education**

Focusing on appropriate consumer understanding of test results rather than curating available tests will allow the FDA to control for undue consumer harm without infringing on consumers’ ability to seek knowledge about their own health. The FDA has the opportunity to hold companies to a high standard for clarity and consumer education while allowing freedom in innovation. For example, a company bringing a new technology to market could be allowed to sell the product with the caveat that the company is responsible for providing clear and easy-to-understand instructions that would prevent a reasonable customer’s misuse of the product. In the case of 23andMe, the company could then have kept its genetic health testing available to consumers, with the knowledge that it would be at fault for a consumer’s reasonable misuse of the information the company provides. In that case, 23andMe would be liable for, and thus take steps to prevent, a reasonable consumer’s misunderstanding of information that could lead to harm. The fear of unnecessary mastectomies in response to a genetic health test indicating high risk for breast cancer would be mitigated, as would the fear of other adverse and inappropriate consumer reactions. The FDA can keep a flexible regulatory framework that allows for innovation and still protects consumers as required by its Congressional mandate by explicitly charging companies with the requirement of adequate consumer education.
VI. Conclusion

In 2007, 23andMe began offering its Personal Genome Service, at the time simply an ancestry test. The company later began offering genetic health testing in addition to its ancestry testing. Its current product offering is its original Ancestry service and its dual Health + Ancestry service. The company allows its customers to opt-into research studies. 23andMe uses its large database containing the genetic and health information of opted-in customers to drive genetic and health research much more quickly than traditional research methods are able.

FDA regulations automatically required 23andMe’s Health service to receive premarket approval as a novel medical device. 23andMe, after months without responding to FDA communications, finally received an official warning letter forcing the halt of sales of any health-related tests. The warning letter was deserved, because 23andMe had been nonresponsive to FDA requests. However, the halt of 23andMe’s sales of its Health testing resulted in poor consequences for consumers. The temporary end of the Health + Ancestry service led to a market in which consumers wanted to know their genetic health information, yet they had no credible, easily accessible provider. Consumers could receive genetic health tests only through a medical provider or by having their DNA sequenced and then separately explained by a third party. The halt of Health + Ancestry sales also led to 23andMe receiving less genetic data than it otherwise would have. Therefore, the company database is less robust than it otherwise would have been. This harms research efforts by limiting the sample size of studies. It is especially harmful to individuals belonging to ethnic minorities, who are frequently underrepresented in genetic data used for research, as well as individuals with rare conditions.

The FDA has recently begun to incorporate soft law practices into its treatment of genetic health tests. Going forward, the FDA should continue and expand its use of soft law. This favors
a permissionless innovation approach while still securing consumers’ safety. By using soft law to promote flexibility in regulation, the FDA will be able to allocate its resources to their most urgent and efficient uses. This will avoid waste and will make the agency’s regulatory structure more robust as new technologies and innovations continue to appear and be adopted at an increasing rate. A soft law regulatory framework will allow the benefits of innovation, yet will retain the FDA’s ability to enforce rules and punish bad actors.

Congress can also pass a formal law requiring the FDA to take a permissionless innovation approach to the medical device market. An approach of this sort could be designed to shift the FDA’s regulatory structure from pre-market to post-market; products would be assumed to be safe enough for consumers to access unless the FDA could show compellingly that they are not. This will give consumers more autonomy over their choices within the market. As Congress has ultimate power over federal agencies through its lawmaking process, this would prevent innovation-stifling FDA actions. Such a law would need to be specifically-worded to ensure that future Administrations cannot take loose interpretations of the law in order to take unnecessary precautionary measures that would stifle innovation. With proper Congressional action, FDA decision-making would be legally-bound to favor innovation.
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