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RESEARCH REVOLUTION OR STATUS QUO?: THE NEW COMMON RULE AND RESEARCH ARISING FROM DIRECT-TO-CONSUMER GENETIC TESTING

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ABSTRACT

The confluence of the 2017 revisions to the Common Rule and the evolving research model utilizing biospecimens and personal information collected by direct-to-consumer genetic testing companies necessitates a deeper consideration of the present ethical, legal, and regulatory issues that arise from personal genomic research. This Article addresses the question of whether the revised Common Rule appropriately protects individuals who use direct-to-consumer genetic testing services and whose information and biospecimens are used in future research protocols. It concludes that despite extended efforts to revise the Common Rule to address the use of biospecimens in human-subjects research, there is little in the revised Rule to direct or guide direct-to-consumer genetic testing companies to ensure a more robust informed consent process for the use of customers' biospecimens and data.

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TABLE OF CONTENTS

I. INTRODUCTION

In 2008, *Time Magazine* declared "The Retail DNA Test" to be the "Best Invention of the Year."[1] Ushering in a "personal-genomics revolution," new technological advances paved the way for private companies to enter the genetics field and offer individual DNA analysis products that are increasingly affordable and accessible to the public at large.[2] Direct-to-consumer genetic testing companies now allow consumers to send in biospecimens—blood, spit, a cheek swab, or urine. In return, the company provides information, based on genetic and phenotypic analysis, relating to the user's ancestry, physical characteristics, biological preferences, and predisposition for disease. Today, direct-to-consumer genetic tests have become so ubiquitous that they are distributed at NFL football games,[3] advertised as the perfect holiday gift,[4] and featured on popular reality TV and talk shows.[5]

The great wealth of information that can be extracted from a person's biospecimens has proven to be an irresistible and profitable treasure trove of information, not just for individuals who are interested in learning about their ancestry or health, but for investigators and institutions interested in performing scientific research. Direct-to-consumer genetic testing companies have collected biospecimens and analyzed the DNA of millions of individuals over the past decade alone, resulting in massive biobank repositories and information-rich datasets housing extensive genetic information.[6] Noting that "DNA has become a

1. Anita Hamilton, *Best Inventions of 2008*, TIME (Oct. 29, 2008), http://content.time.com/time/specials/packages/printout/0,29239,1852747_1854493_1854113,00.html [https://perma.cc/TT7L-SE72].

2. *Id*.

3. Jeff Barker, *Ravens Fans to Be Offered DNA Test Kits Sunday in Unusual NFL Promotion*, BALT. SUN (Sept. 14, 2017, 6:00 AM), http://www.baltimoresun.com/business/bs-bz-ravens-dna-testing-20170913-story.html [https://perma.cc/SM8L-Q3AQ]; Doug Levy, *You Can Get Your DNA Tested at an NFL Game. Should You?*, NPR (Nov. 8, 2017, 5:00 AM), https://www.npr.org/sections/health-shots/2017/11/08/562564639/you-can-get-your-dna-tested-at-an-nfl-game-should-you [https://perma.cc/24SW-PNNH].

4. Laura Hercher, *Genome Culture: How to Decide Which DNA Tests to Buy*, GENOME (Dec. 7, 2017), http://genomemag.com/2017/12/genome-culture-a-holiday-gift-giving-guide/ [https://perma.cc/3AN2-F7K2] ("Evaluating direct-to-consumer kits for tucking under your family tree."); *TODAY's Biggest Holiday Guide Ever: Google Home Mini and More*, TODAY (Dec. 12, 2017), https://www.today.com/video/today-s-biggest-holiday-guide-ever-google-home-mini-and-more-1114650179691 [https://perma.cc/A9T2-ZH3Z] (recommending 23andMe's ancestry service as a great holiday gift).

5. *The View Co-hosts and Caitlyn Jenner Find Out 23andMe Results* (ABC television broadcast July 14, 2017), http://abc.go.com/shows/the-view/video/pl5554876/VDKA3969391 [https://perma.cc/2PUB-6G2H].

6. *See, e.g.*, *What Happens to Your Genetic Data When You Take a Commercial DNA Ancestry Test?*, CITIGEN (Dec. 07, 2017), http://www.citigen.org/2017/07/12/what-happens-

commodity sought by scientists and biotech companies," it was reported that, in 2017, the number of individuals who utilized direct-to-consumer genetic tests more than doubled.[7]

Research using these biospecimens and the information associated with them is revolutionizing the model for genetic research.[8] In 2012, one of the Authors addressed the then-current state of direct-to-consumer genetic testing services and revealed challenges that are not addressed by our current regulatory framework.[9] In particular, the Author concluded that whether research arising from direct-to-consumer genetic testing companies is subject to the Common Rule—the set of regulations that govern the majority of research involving human subjects in the United States—remained unsettled.[10]

Since then, the market for direct-to-consumer genetic testing has continued to grow and expand. More companies offer greater—and often cheaper—opportunities for individuals to utilize these companies' services, leading to an increasing amount of information being collected and stored for research purposes. Some companies have made it much more explicit that they intend to use biospecimens collected during the direct-to-consumer testing process for research, acknowledging the significant financial benefits of doing so.[11]

Beginning in 2011 and culminating in early 2016, the U.S. Department of Health and Human Services engaged in the process of updating and revising the Common Rule in response to the transforming and expanding research enterprise.[12] Its stated goal was to increase protections for research participants while reducing burden, delay, and ambiguity for investigators.[13] During

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to-your-genetic-data-when-you-take-a-commercial-dna-ancestry-test/ [https://perma.cc/XH7F-E2WT].

7. Antonio Regalado, *2017 Was the Year Consumer DNA Testing Blew Up*, MIT TECH. REV. (Feb. 12, 2018), https://www.technologyreview.com/s/610233/2017-was-the-year-consumer-dna-testing-blew-up/ [https://perma.cc/C643-28QQ].

8. *See* Valerie Gutmann Koch, *PGTandMe: Social Networking-Based Testing and the Evolving Research Model*, 22 HEALTH MATRIX 33, 47–50 (2012) (discussing the role of online social networks in accessing new research populations).

9. *See generally id*.

10. *Id*. at 57.

11. *See* Matthew Herper, *Surprise! With $60 Million Genentech Deal, 23andMe Has a Business Plan*, FORBES (Jan. 6, 2015, 9:58 AM), https://www.forbes.com/sites/matthewherper/2015/01/06/surprise-with-60-million-genentech-deal-23andme-has-a-business-plan/#2364601c2be9 [https://perma.cc/82XC-A4JZ].

12. Jerry Menikoff et al., *The Common Rule, Updated*, 376 NEW ENG. J. MED. 613, 613 (2017).

13. Human Subjects Research Protections, 76 Fed. Reg. 44512, 44514 (proposed July 26, 2011) (to be codified at 45 C.F.R. pts. 46, 160, & 164).

this process, it released two sets of proposals—an Advanced Notice of Proposed Rule Making (ANPRM) and Notice of Proposed Rule Making (NPRM)—that attempted to address the lack of clarity and consistency related to the regulation of research involving human biospecimens and information.[14] In other words, the ANPRM and NPRM proposed approaches to regulating exactly the type of research that arises from samples and data collected through direct-to-consumer genetic testing.[15]

The confluence of the revisions to the Common Rule and the evolving research model utilizing biospecimens and personal information collected by direct-to-consumer genetic testing companies necessitates a deeper consideration of the present ethical, legal, and regulatory issues that arise from personal genomic research. This article addresses the question of whether the revised Common Rule appropriately protects individuals who consume direct-to-consumer genetic testing services and whose information and biospecimens are used in future research protocols.

Part II of this Article addresses the evolution of consumer genomics and includes a summary of the direct-to-consumer genetic testing products currently on the market, with respect to both the testing services available and the companies' stated intentions to use biological samples and data for research purposes. Part III surveys how direct-to-consumer genetic testing companies currently ensure (or fail to ensure) informed consent from their customers. Part IV describes the current state of regulation of research utilizing biospecimens and data collected from direct-to-consumer genetic testing services. Part V evaluates how the revised Common Rule will apply to research conducted by these companies utilizing customers' biospecimens and personal information. The Article concludes that the revised Common Rule enables these direct-to-consumer genetic testing companies to more easily perform secondary research utilizing customers' biospecimens and data while doing little to regulate or guide these companies in conducting ethical research or protecting participant

14. *Id*. Federal Policy for the Protection of Human Subjects, 80 Fed. Reg. 53933 (proposed Sept. 8, 2015) (to be codified at 45 C.F.R. pt. 46).

15. The final rule regulates research using "identifiable biospecimen[s]," a biological sample "for which the identity of the subject is or may readily be ascertained." Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149, 7260 (proposed Jan. 19, 2017) (to be codified at 45 C.F.R. pt. 46). Such information is necessarily generated and stored by direct-to-consumer companies as part of their services. *See, e.g.*, Pascal Su, *Direct-to-Consumer Genetic testing: A Comprehensive View*, 86 YALE J. BIOLOGY & MED. 359, 362 (2013).

autonomy.

II. THE RISE OF CONSUMER GENOMICS

A. Direct-to-Consumer Genetic Testing

Although around 99.9 percent of all human DNA is genetically identical, the remaining 0.1 percent varies, dictating the biological attributes that make an individual distinct.[16] DNA is composed of nucleotides consisting of deoxyribose sugars and phosphate groups that are attached to nitrogenous bases.[17] Through phosphodiester bonds, the phosphate group of one nucleotide attaches to the sugar of another nucleotide, creating long polynucleotide chains that form the sugar-phosphate "backbone" of DNA.[18] The familiar double helix is created by the nitrogen bases of one chain attaching through hydrogen bonds to the nitrogen bases of another chain.[19] The sequence of these nitrogen base pairings are what is transcribed by RNA and translated to direct the creation of a specific protein molecule.[20]

The human genome contains approximately three billion base pairs.[21] These bases—adenine, cytosine, guanine, and thymine—make up complementary strands of DNA that, wound into the double helix structure, are arranged in twenty-three pairs of chromosomes.[22] An individual's genotype, his or her unique sequence of base pairings, is constituted of the two independent versions of the gene that the person inherited.[23] The specific

16. Marla Vacek Broadfoot, *Variation in "Junk" DNA Leads to Trouble*, DUKE TODAY (Aug. 30, 2016), https://today.duke.edu/2016/08/variation-%E2%80%9Cjunk%E2%80%9D-dna-leads-trouble [https://perma.cc/YU54-TXMY].

17. *Essentials of Genetics: DNA Is a Structure That Encodes Biological Information*, SCITABLE, https://www.nature.com/scitable/ebooks/essentials-of-genetics-8/126430897#bookContentViewAreaDivID%20(last%20visited%20July%2014,%202017 [https://perma.cc/G4W8-ZHE3] (last visited Aug. 18, 2018).

18. *Id*.

19. *Id*.

20. *Essential of Genetics: The Information in DNA Is Decoded by Transcription*, SCITABLE, https://www.nature.com/scitable/ebooks/essentials-of-genetics-8/126042256#bookContentViewAreaDivID [https://perma.cc/NK49-NT4L] (last visited Aug. 18, 2018).

21. *The Human Genome Project Completion: Frequently Asked Questions*, NAT'L HUMAN GENOME RES. INST., https://www.genome.gov/11006943/human-genome-project-completion-frequently-asked-questions/ [https://perma.cc/Q5U3-WV2Z] (last updated Oct. 30, 2010).

22. *Id*.

23. *Inheritance Patterns—Phenotype and Genotype*, JRANK: MED. ENCYCLOPEDIA, http://medicine.jrank.org/pages/2449/Inheritance-Patterns-Phenotype-Genotype.html [https://perma.cc/GS8K-KY4M] (last visited Aug. 17, 2018).

sequence of the nitrogenous base pairings dictates the creation of proteins, which make up organs and tissue and control chemical reactions and signaling.[24] The chromosomes that make up the human genome contain about twenty thousand of these protein-coding regions, which are referred to as genes.[25] Together with environmental factors, one's genes determine his or her phenotype, the physical manifestation of the genotype.[26] Phenotypic expression includes not only the specific proteins that are coded for by a gene but the large-scale, observable features they produce, such as eye color or the shape of one's ears.[27] One's genes can predispose an individual to many common diseases, such as cancer, diabetes, cardiovascular disease, and asthma.[28]

The most common types of genetic variations are single nucleotide polymorphisms (SNPs), which occur about once in every 300 base pairs.[29] These alterations to a single base pair can occur in both non-coding regions and protein-coding gene regions of the DNA.[30] While an SNP occurring within a gene or a related regulatory region may play a direct role in the development of a certain disease, SNPs are inherited and can also be used as linear indicators of the risk profile associated with a certain heritable disease.[31]

These SNPs are what many major genetic testing companies use to analyze DNA samples. For example, one of the largest direct-to-consumer genetic testing companies, 23andMe, identifies the genotype of its customers using microarray genotyping.[32]

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24. *A Brief Guide to Genomics*, NAT'L HUMAN GENOME RES. INST., https://www.genome.gov/18016863/a-brief-guide-to-genomics/ [https://perma.cc/H4A2-9GT4] (last updated Aug. 27, 2015).

25. Iakes Ezkurdia et al., *Multiple Evidence Strands Suggest That There May Be as Few as 19000 Human Protein-Coding Genes*, 23 HUM. MOLECULAR GENETICS 5866, 5873 (2014).

26. *Inheritance Patterns*, *supra* note 23.

27. *Id*.

28. *Genes and Human Disease: Genes and Noncommunicable Diseases*, WORLD HEALTH ORG., http://www.who.int/genomics/public/geneticdiseases/en/index3.html [https://perma.cc/8GTD-JLVP] (last visited Aug. 19, 2018). For a list of genetic disorders, see *Specific Genetic Disorders*, NAT'L HUMAN GENOME RES. INST., https://www.genome.gov/10001204/specific-genetic-disorders/ [https://perma.cc/69TR-LDUW] (last reviewed May 18, 2018).

29. *What Is Genetic Variation?*, YOURGENOME, http://www.yourgenome.org/facts/what-is-genetic-variation [https://perma.cc/R5LS-YEFL] (last updated Feb. 4, 2015).

30. *SNP*, SCITABLE, https://www.nature.com/scitable/definition/single-nucleotide-polymorphism-snp-295 [https://perma.cc/J9GU-2TCX] (last visited Aug. 16, 2018).

31. *What Are Single Nucleotide Polymorphisms (SNPs)?*, U.S. NAT'L LIBRARY OF MED., https://ghr.nlm.nih.gov/primer/genomicresearch/snp [https://perma.cc/4YGU-Z6G3] (last updated Aug. 14, 2018).

32. *Understanding the Different Versions of the 23andMe Genotyping Chip*,

When a customer purchases a test from 23andMe and submits a saliva sample, the company tests for specific genetic variants.[33] Using similar microarray technology, AncestryDNA surveys an individual's genome at over seven hundred thousand locations.[34] In addition to SNPs, AncestryDNA looks for insertion/deletion polymorphisms (indels),[35] variations found throughout the genome where either a specific nucleotide base pair has been added or deleted.[36] Together, SNPs and indels account for more than ninety-nine percent of genetic variation.[37]

Other direct-to-consumer genetic testing companies offer more extensive exome sequencing. The exome is made up of the protein-coding regions of the DNA and contains about eighty-five percent of known disease-variants.[38] Unlike genotyping, whole-exome sequencing identifies the exact sequence of nucleotides that make up a given section of DNA.[39] By sequencing an entire exome, a company can not only identify known genotypic variants but also variants that are unique to that individual's DNA.[40] In 2012, 23andMe announced an initiative to move into the field of whole-exome sequencing,[41] although its effort was ultimately abandoned in 2016.[42] Other companies, such as Genos, continue to offer direct-

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23ANDME, https://customercare.23andme.com/hc/en-us/articles/218392668Understanding-the-different-versions-of-the-23andMe-genotyping-chip [https://perma.cc/AFM8-P6D5] (last visited Aug. 16, 2018).

33. *How Does 23andMe Genotype My DNA?*, 23ANDME, https://customercare.23andme.com/hc/en-us/articles/202904610-How-does-23andMe-genotype-my-DNA- [https://perma.cc/87XG-EU9Z] (last visited Aug. 16, 2018).

34. *AncestryDNA—Frequently Asked Questions (United States)*, ANCESTRY, https://www.ancestry.com/dna/en/legal/us/faq [https://perma.cc/4A2K-LG7J] (last visited Aug. 16, 2018).

35. *Id*.

36. Laura Rodriquez-Murillo & Rany M. Salem, *Insertion/Deletion Polymorphism*, ENCYCLOPEDIA OF BEHAV. MED. (Marc D. Gellman & J. Rick Turner eds., 2013), https://link.springer.com/referenceworkentry/10.1007%2F978-1-4419-1005-9_706 [https://perma.cc/9PMD-Q6M9].

37. The 1000 Genomes Project Consortium, *A Global Reference for Human Genetic Variation*, 526 NATURE 68, 68 (2015).

38. Bahareh Rabbani et al., *The Promise of Whole-Exome Sequencing in Medical Genetics*, 59 J. HUM. GENETICS 5, 5 (2014).

39. *See What is the Difference Between Genotyping and Sequencing?*, 23ANDME, https://customercare.23andme.com/hc/en-us/articles/202904600-What-is-the-difference-between-genotyping-and-sequencing- [https://perma.cc/YRT6-432C] (last visited Aug.. 16, 2018).

40. *Id*.

41. *23andMe Moves into the World of Sequencing*, 23ANDMEBLOG (Nov. 2, 2012), https://blog.23andme.com/23andme-research/23andme-moves-into-the-world-of-sequencing/ [https://perma.cc/6QU5-SDSQ].

42. Sarah Buhr, *23andMe Reportedly No Longer Working on Next-Gen Sequencing*, TECHCRUNCH (Oct. 26, 2016), https://techcrunch.com/2016/10/26/23andme-reportedly-laid-off-nearly-half-a-dozen-staff-working-on-next-gen-sequencing/[https://perma.cc/9KH9-

to-consumer DNA sequencing.[43] Helix, an Illumina-backed start-up, offers a similar test that also sequences certain non-coding areas that the company has identified as being "information-rich."[44] In 2017, Helix launched an "app store for [the] genome," which enables users to access information about their genetic makeup using various applications developed by third parties.[45] Veritas Genetics offers one of the most extensive direct-to-consumer genetic testing services on the market: full-genome sequencing for nine hundred ninety-nine dollars.[46] While Veritas requires a doctor's order form, it still reports results directly to the consumer through a smartphone-friendly report.[47]

As technology has improved and decreased the costs associated with genetic testing, more companies have entered the genomics field, thereby increasing competition for direct-to-consumer genetic services. For 23andMe, these technological advances have allowed it to genotype more than five million customers.[48] AncestryDNA, the largest consumer genetic testing company, surpassed four million genotyped customers in April 2017.[49] As costs continue to decrease, some researchers suggest that the rate of genetic testing will continue its meteoric rise, predicting that one hundred million to two billion human genomes will be sequenced by 2025.[50] This increase in competition and interest in direct-to-consumer genetic testing services has also initiated an economic boom, with some predicting that the global market for direct-to-consumer genetic testing will increase twelve percent by 2021.[51]

A623].

43. *Get a Running Start,* GENOS, https://genos.co/order.html [https://perma.cc/P9E7-K6E8] (last visited Aug. 19, 2018).

44. *See What Is Helix?*, HELIX: HELIX BLOG (July 10, 2017), https://blog.helix.com/what-is-helix/ [https://perma.cc/8ZQ8-4J6J].

45. Emily Mullin, *A DNA App Store is Here, But Proceed with Caution*, MIT TECH. REV. (July 24, 2017), https://www.technologyreview.com/s/608313/a-dna-app-store-is-here-but-proceed-with-caution/amp/ [https://perma.cc/HJ8L-FSQ6].

46. *My Genome*, VERITAS, https://www.veritasgenetics.com/mygenome [https://perma.cc/8XUG-XVEJ] (last visited Aug. 16, 2018).

47. *Id*.

48. *About Us*, 23ANDME, https://mediacenter.23andme.com/company/about-us/ [https://perma.cc/ZH8C-MRDV] (last visited Aug. 16, 2018).

49. Ancestry Team, *AncestryDNA Reaches 4 Million Customers in DNA Database*, ANC.: ANC. BLOG (Apr. 27, 2017), https://blogs.ancestry.com/ancestry/2017/04/27/ancestry dna-reaches-4-million-customers-in-dna-database/ [https://perma.cc/673T-FDNN].

50. Erika Check Hayden, *Genome Researchers Raise Alarm over Big Data*, NATURE: NEWS (July 7, 2015), http://www.nature.com/news/genome-researchers-raise-alarm-over-big-data-1.17912# [https://perma.cc/BUR9-TVD8].

51. *Global Direct-to-Consumer Genetic Testing Market – Forecasts, Segmentation, and Opportunity Assessment by Technavio*, BUS. WIRE (Aug. 1, 2017, 3:23 PM),

B. Consumer Genomics in Research

The proliferation of personal genetic testing has resulted in the formation of massive caches of biospecimens and datasets of genetic information. After receiving a customer's biological sample, direct-to-consumer genetic testing companies run their analyses and report to their customers the information on ancestry, wellness, carrier status, traits, or risk profiles for certain genetic diseases.[52] Although these reports may provide useful, entertaining, or just benign information to the customer, the actual genetic information that these companies collect during their analyses is much more robust.[53] Genetic data, with its biologically-rich map for human life, presents a treasure trove of information for scientific researchers.

Genetic testing companies themselves can conduct research utilizing customers' biospecimens and data. They can also maintain and store physical samples in biobanks, or repositories of biological specimens, which can be studied to identify gene variations associated with human diseases or traits. Access to these biobanks enables a company and its partners to conduct secondary research on the biological samples that were collected in the course of providing a service for consumers. Much of this future research is unanticipated and unidentified at the time the biospecimens are first collected. However, secondary research on these biospecimens may offer "substantial public benefit" and be of "enormous value."[54] A better understanding of the genetic underpinnings of a condition can shed light on its etiology and risk profile and help bring accuracy to medical diagnosis and treatment.

In recent years, improvements in sequencing technology and the increased availability of genetic data have also brought life to the precision medicine movement. In 2015, President Barack Obama launched the Precision Medicine Initiative, a long-term research effort of the National Institutes of Health to determine how genetic information can be used to better diagnose and treat

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http://www.businesswire.com/news/home/20170801006055/en/ [https://perma.cc/NPT6-77XW].

52. *Find Out What Your DNA Says About Your Health, Traits and Ancestry*, 23ANDME, https://www.23andme.com/dna-health-ancestry/ [https://perma.cc/EA2Y-AZUA] (last visited Aug. 16, 2018).

53. *See* Kayte Spector-Bagdady, Commentary, *"The Google of Healthcare": Enabling the Privatization of Genetic Bio/Databanking*, 26 ANNALS OF EPIDEMIOLOGY 515, 515–16 (2016).

54. Holly Fernandez Lynch et al., *Confronting Biospecimen Exceptionalism in Proposed Revisions to the Common Rule*, 46 HASTINGS CTR. REP. 4, 4–5 (2016).

individuals afflicted by a range of diseases.[55] Around the same time, Vice President Joe Biden established the Cancer Moonshot, with the goal of removing uncertainty from cancer treatment by offering patients unique cures targeted to their specific genetic makeup.[56] Developing targeted drugs and identifying biomarkers that are indicative of a therapeutic response to a disease is challenging and requires large volumes of genetic data.[57]

Personal genetic testing companies are able to meet the needs of modern genetic research as they collect massive datasets that can be used to create generalizable results.[58] Direct-to-consumer genetic testing companies like 23andMe and AncestryDNA have spent years not only collecting and amassing large collections of genetic data, but have done so using a business model in which the consumers pay for services that enable the companies to collect, store, and conduct research utilizing their DNA.[59] According to 23andMe board member Patrick Chung, the company's "long game . . . is not to make money selling kits, although the kits are essential to get the base level data."[60] In fact, a significant portion of these companies' profits come not "from the sale of genetic tests, but from gathering genetic and personal data that can be licensed or sold to institutions, academic researchers, [and] drug companies."[61]

Once a company has access to an individual's genetic data, the

55. *Fact Sheet: President Obama's Precision Medicine Initiative*, WHITE HOUSE, OFFICE OF THE PRESS SEC'Y (Jan. 30, 2015), https://obamawhitehouse.archives.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative [https://perma.cc/HUZ6-89AX].

56. *Fact Sheet: Vice President Biden Delivers Cancer Moonshot Report, Announces Public and Private Sector Actions to Advance Cancer Moonshot Goals*, OFFICE OF THE VICE PRESIDENT (Oct. 17, 2016), https://obamawhitehouse.archives.gov/the-press-office/2016/10/17/fact-sheet-vice-president-biden-delivers-cancer-moonshot-report [https://perma.cc/94PL-ADU8]; Catherine Offord, *Pharma Cooperates to Achieve Precision Medicine*, THESCIENTIST (Feb. 1, 2017), http://www.the-scientist.com/?articles.view/articleNo/48070/title/Pharma-Cooperates-to-Achieve-Precision-Medicine/ [https://perma.cc/Z649-ANFC].

57. Offord, *supra* note 56.

58. Barbara J. Evans, *Power to the People: Data Citizens in the Age of Precision Medicine*, 19 VAND. J. ENT. & TECH. L. 243, 244 (2016).

59. Katie M. Palmer, *Another Personal Genetics Company is Sharing Client Data*, WIRED (July 21, 2015, 9:00 AM), https://www.wired.com/2015/07/another-personal-genetics-company-selling-client-data/ [https://perma.cc/K57D-RN8P].

60. Michael Grothaus, *How 23andMe is Monetizing your DNA*, FAST COMPANY (Jan. 5, 2015), https://www.fastcompany.com/3040356/what-23andme-is-doing-with-all-that-dna [https://perma.cc/78SN-6TMX] (Chung envisioned that 23andMe could "become the Google of personalized health care.").

61. Koch, *supra* note 8, at 50.

information can ostensibly be analyzed *ad infinitum*.[62] One person's data can therefore be used in a wide range of studies conducted at different times or by different researchers, with little or no contact between the scientists and the participants. Under traditional research protocols, the recruitment of research participants can be a challenge for researchers, with studies often being delayed due to low enrollment.[63] It can also take significant "cajoling to get people . . . to part ways with their biological bits."[64] Having access to a pre-existing bank of genetic information therefore greatly reduces the time, effort, and cost of recruitment for researchers in the genetics field.[65] 23andMe's databank allows the company to undertake "real-time research initiatives" and "eliminates recruitment times, minimizes cost, and reduces the amount of time it takes to conduct research."[66] Whereas a traditional study into genetic variants would likely take "months and thousands of dollars," according to 23andMe Vice President of Communications, Angela Calman-Wonson, the same study can be performed by 23andMe in "about 48 hours."[67]

Moreover, personal genetic testing companies have tapped into the power of social networking.[68] Online networking sites that emphasize health information create a community of individuals who can readily be targeted for specific research needs.[69] This manner of "crowd-sourcing" recruitment connects companies with "highly engaged populations with specific medical conditions."[70] Personal genetic testing companies have created online forums and communities for customers to share their results, learn about their genetic variants, and connect with others who share similar ancestry or health biomarkers.[71] Tapping into this crowd-sourced data enables companies to engage in research that otherwise would not have been feasible.[72]

62. *Id*. at 51.
63. *Id*. at 47.
64. Palmer, *supra* note 59.
65. *See id*.
66. Grothaus, *supra* note 60.
67. *Id*.
68. Koch, *supra* note 8, at 49.
69. *Id*. at 48.
70. *Id*. at 49.
71. *See Accessing the 23andMe Forums*, 23ANDME, https://customercare.23andme.com/hc/en-us/articles/215644387-Accessing-the-23andMe-forums [https://perma.cc/6MBM-4PZZ] (last visited Aug. 17, 2018) ("The 23andMe Forums are a place to form connections with fellow customers, ask and answer questions, and gain a better understanding of what you can learn from the 23andMe service.").
72. Grothaus, *supra* note 60.

The pool of information available to personal genetic testing companies is not limited to genetic information. In conjunction with genotyping or sequencing services, many personal genetic testing companies also collect self-reported information from their customers through questionnaires and surveys.[73] Helix's Platform Consent identifies this information as any "details about you that aren't a part of your DNA," including "details about your health, family tree, lifestyle, and behaviors."[74] Similarly, 23andMe collects information about its customers' "disease conditions, other health-related information, personal traits, ethnicity, family history," and more.[75] Combining genetic data with this self-reported information creates a more dynamic and valuable dataset than either type of information analyzed alone.

These repositories of biological data place personal genetic testing companies in a prime position to conduct "work in sequencing, imputation, multi-variant modeling for risk predictions and therapeutics," while their status as a service provider allows them to seek out valuable, targeted demographics.[76] For example, through a partnership with the Michael J. Fox Foundation, 23andMe recruited more than ten thousand individuals with Parkinson's disease to its database by offering its genetic testing services free of charge.[77] The initiative allowed 23andMe to establish the largest community for Parkinson's research in the world.[78] In a similar effort to address the underrepresentation of African American data in genetic research, 23andMe was recently awarded a 1.7 million-dollar grant from the National Institutes of Health's National Human Genome Research Institute.[79] The partnership allowed 23andMe

73. Katherine Drabiak, *Caveat Emptor: How the Intersection of Big Data and Consumer Genomics Exponentially Increases Informational Privacy Risks*, 27 HEALTH MATRIX 143, 148, 154 (2017).

74. *Helix Platform Consent*, HELIX, https://www.helix.com/platform-consent [https://perma.cc/8CAM-8BJ5] (last modified June 22, 2018).

75. *Privacy Highlights*, 23ANDME, https://www.23andme.com/about/privacy/ [https://perma.cc/JX9B-UGQ4] (last updated May 24, 2018) [hereinafter *Privacy Highlights*].

76. *See 23andMe Genome Research Day*, 23ANDMEBLOG (June 7, 2017), https://blog.23andme.com/news/inside-23andme/23andme-genome-research-day/ [https://perma.cc/XMG8-XQ5P].

77. *Michael J. Fox Foundation Brings Parkinson's Data to tranSMART*, BIO-IT WORLD (May 15, 2015), http://www.bio-itworld.com/2015/5/15/michael-j-fox-foundation-brings-parkinsons-data-transmart.html [https://perma.cc/88WL-KSG9].

78. *The Search for a Cure Starts with your DNA*, 23ANDME, https://www.23andme.com/pd/ [https://perma.cc/MR5N-TF3J] (last visited Aug. 18, 2018).

79. *23andMe Receives $1.7M NIH Grant to Create Sequencing Panel for African Americans*, GENOMEWEB (Oct. 13, 2016), https://www.genomeweb.com/sequencing/23and

to launch the African Genetics Project, an effort to diversify genetic research by offering free kits to individuals with close ties to sub-Saharan Africa.[80]

These direct-to-consumer genetic testing companies often serve as the gatekeepers to databanks of genetic and personal information—partnering with companies and academic researchers to conduct research. For example, in 2014, 23andMe announced a partnership with pharmaceutical giant Pfizer to study inflammatory bowel disease.[81] The partnership has since expanded into other areas as well, with one recent study becoming the largest yet to look into the genetic causes of depression.[82] In the past few years, 23andMe has also entered into a sixty-million-dollar partnership with Genentech to study Parkinson's disease, a deal which some suggest singlehandedly "could generate almost as much revenue as doubling 23andMe's customer base."[83] As of 2016, 23andMe had "access agreements with 30 pharmaceutical and biotech companies . . . in addition to partnerships with academic and nonprofit organizations."[84] By late 2017, the company reported that it had over "50 active collaborations," developed through a "formal process" of soliciting and vetting academic research proposals.[85] And in July 2018, 23andMe announced its partnership with GlaxoSmithKline, which will allow the drug develop drugs based on DNA and other information collected from the direct-to-consumer genetic testing company's five million customers.[86]

Utilizing its vast consumer databases, 23andMe has

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me-receives-17m-nih-grant-create-sequencing-panel-african-americans [https://perma.cc/556K-T7S9].

80. *The African Genetics Project*, 23ANDMEBLOG (Oct. 12, 2016), https://blog.23andme.com/23andme-research/the-african-genetics-project/ [https://perma.cc/MT8S-GEV3].

81. *23andMe Announces Agreement with Pfizer Inc. to Research Genetics of Ulcerative Colitis and Crohn's Disease*, 23ANDME (Aug. 12, 2014), https://mediacenter.23andme.com/press-releases/23andme-announces-agreement-with-pfizer-inc-to-research-genetics-of-ulcerative-colitis-and-crohns-disease/ [https://perma.cc/EJ9X-UGCE].

82. *See* Antonio Regalado, *23andMe Pulls Off Massive Crowdsourced Depression Study*, MIT TECH. REV. (Aug. 1, 2016), https://www.technologyreview.com/s/602052/23andme-pulls-off-massive-crowdsourced-depression-study/ [https://perma.cc/ZJM6-HXLR].

83. Herper, *supra* note 11.

84. Spector-Bagdady, *supra* note 53, at 516.

85. Catherine Offord, *The Rising Research Profile of 23andMe*, THESCIENTIST (Dec. Nov. 30, 2017), https://www.the-scientist.com/?articles.view/articleNo/51073/title/The-Rising-Research-Profile-of-23andMe/ [https://perma.cc/V3VB-UJ6V].

86. Maggie Fox, *Drug Giant Glaxo Teams Up with DNA Testing Company 23andMe*, NBC NEWS (July 25, 2018), https://www.nbcnews.com/health/health-news/drug-giant-glaxo-teams-dna-testing-company-23andme-n894531?cid=sm_npd_nn_tw_ma [https://perma.cc/K8MW-VTC4].

published over one hundred papers since 2010.[87] Its research team has more than doubled from 2015 to 2017.[88] The company estimates that a single individual's information "contributes to over 230 studies on topics that range from Parkinson's disease to lupus to asthma and more."[89]

And 23andMe is not the only company pursuing such research endeavors. AncestryDNA has announced a partnership with Calico, a research and development company that focuses on longevity, "to investigate human heredity of lifespan."[90] Veritas Genetics' partners include the Harvard Medical School Personal Genome Project.[91]

III. DIRECT-TO-CONSUMER GENETIC TESTING COMPANIES' APPROACH TO INFORMED CONSENT

A. Informed Consent to Research

As consumers pursue direct-to-consumer genetic testing, questions arise about the nature and scope of the research conducted by the companies that offer these tests, as well as their partners.[92] One of the greatest concerns is whether customers are adequately informed that their biospecimens may be used in research, that they understand the associated risks, and that they voluntarily decide to allow their biospecimens to be used in research.

Informed consent—the key method by which autonomy is

87. *Publications*, 23ANDME, https://www.23andme.com/publications/ [https://perma.cc/JPD6-AVRR] (last visited Aug. 18, 2018).

88. *See* Offord, *supra* note 85.

89. *Research*, 23ANDME, https://www.23andme.com/research/ [https://perma.cc/UM3F-CHKC] (last visited Aug. 18, 2018).

90. *AncestryDNA and Calico to Research the Genetics of Human Lifespan*, CALICO (July 21, 2015), https://www.calicolabs.com/news/2015/07/21/ [https://perma.cc/F3GQ-W3VS].

91. *Veritas Genetics Partners with PGP to Offer $1K Genome*, GENOMEWEB (Sept. 29, 2015), https://www.genomeweb.com/business-news/veritas-genetics-partners-pgp-offer-1k-genome [https://perma.cc/D7HN-UT7R].

92. Heidi C. Howard et al., *The Convergence of Direct-to-Consumer Genetic Testing Companies and Biobanking Activities*, *in* KNOWING NEW BIOTECHNOLOGIES: SOCIAL ASPECTS OF TECHNOLOGICAL CONVERGENCE 66–67 (Matthias Weinroth & Eugenia Rodrigues eds., 2015); Heidi C. Howard et al., *Blurring Lines*, 11 EUR. MOLECULAR BIOLOGY ORG. REP. 579, 579 (2010); Koch, *supra* note 8, at 50; Emilia Niemiec et al., C*ontent Analysis of Informed Consent for Whole Genome Sequencing Offered by Direct-to-Consumer Genetic Testing Companies*, 37 HUM. MUTATION 1248, 1254 (2016); Spector-Bagdady, *supra* note 53, at 516; Marcy Darnovsky, Opinion, *23andMe's Dangerous Business Model*, N.Y. TIMES (Mar. 2, 2015, 3:30 AM), https://www.nytimes.com/roomfordebate/2015/03/02/23andme-and-the-promise-of-anonymous-genetic-testing-10/23andmes-dangerous-business-model-17.

recognized in the research context—is essential to the conduct of ethical research.[93] However, studies of direct-to-consumer genetic testing companies' approach to informed consent in research have concluded that "it is clear that the consent procedure currently used is ethically inadequate."[94]

Direct-to-consumer genetic testing companies have ever-changing and sometimes conflicting methods of obtaining consent. Among the approaches to consent—albeit the one that appears to be used least—is requesting individual-level consent for an identified research purpose. For example, a recent partnership between 23andMe and Genentech aimed at identifying new therapeutic targets for treating Parkinson's disease analyzes the health and genetic data of participants on an individual, as opposed to an aggregated, level.[95] Together, the partners are working to generate whole genome sequencing data for three thousand individuals who either have Parkinson's disease or have a family member with the disease.[96] Because this more invasive analysis falls outside the scope of the company's Privacy Policy and Terms and Conditions, 23andMe obtained additional consent to participate in the research from each individual participant that was recruited to the study.[97]

Other personal genetic testing companies have engaged in a similar study-specific approach to informed consent to research. Genos, a consumer spinoff of Complete Genomics that began beta testing in 2016,[98] offers a personal genetic testing service that is overtly intertwined with research. For a fee, Genos will sequence

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93. Donna M. Gitter, *Informed Consent and Privacy of Non-Identified Bio-Specimens and Estimated Data: Lessons from Iceland and the United States in an Era of Computational Genomics*, 38 CARDOZO L. REV. 1251, 1262, 1270 (2017).

94. Sigrid Sterckx et al., *"Trust is Not Something You Can Reclaim Easily": Patenting in the Field of Direct-to-Consumer Genetic Testing*, 15 GENETICS IN MED. 382, 385 (2013) (addressing consent in the context of disclosure of company patent activity: "Participants may consent to donate biological materials and phenotypic data for the development of clinical applications. However, if they are not aware that this might be happening through commercialization involving patents, this might undermine the original trust and show the original consent to be invalid since participants were not told clearly 'what it was about' and hence were not able to make 'their own informed decisions to join or not'").

95. *See 23andMe and Genentech to Analyze Genomic Data for Parkinson's Disease*, 23ANDME (Jan. 6, 2015), https://mediacenter.23andme.com/press-releases/23andme-genentech-pd/ [https://perma.cc/M4BB-HJZF]; Herper, *supra* note 11.

96. *See id*.

97. Sarah Zhang, *Of Course 23andMe's Plan Has Been to Sell Your Genetic Data All Along*, GIZMODO (Jan. 6, 2015, 3:35 PM), http://gizmodo.com/of-course-23andmes-business-plan-has-been-to-sell-your-1677810999 [https://perma.cc/R43Y-NS7V].

98. Julia Karow, *Consumer Genomics Startup Genos Research Plans to Let Customers Explore, Share Their Data*, GENOMEWEB (June 13, 2016), https://genos.co/public-assets/press/GenosReprintGenomeWeb.pdf [https://perma.cc/6KTM-D7TW].

a customer's entire exome and deliver a report detailing certain medical implications of the individual's specific genetic variants.[99] Upon delivering this report, Genos acts as a sort of scientific research broker by advertising different genetic research opportunities in which its customers can participate.[100] Genos customers can elect to share its genetic data with a particular investigator for a particular study by signing a specific informed consent and in return will be compensated between fifty and two hundred dollars per project.[101]

In contrast, some direct-to-consumer genetic testing companies seek broad consent to use an individual's identifiable biospecimens or data for undefined future research purposes. For example, 23andMe's research arm, 23andMe Research, allows customers to volunteer to donate their genetic information, self-reported information, and other personal data to the company's research efforts.[102] According to 23andMe's Research Consent form, biospecimens and data are collected to facilitate research on the "genetic factors behind diseases and traits"; the "connections among diseases and traits"; the genetic underpinnings of "human migration and population history"; and "how people react to their personal genetic information."[103] By agreeing to participate in 23andMe Research, a customer consents to the company's "use [of his or her] data for research that will be published in scientific journals, or that is sponsored by the National Institutes of Health and certain other organizations."[104] This includes research that is performed by 23andMe, as well as research that is "sponsored by or conducted on behalf of third parties, such as non-profit foundations, academic institutions or pharmaceutical companies."[105]

23andMe's Research Consent addresses the expected benefits and risks of participation. As with all research protocols, the

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99. *Id*.

100. Megan Molteni, *Genos Will Sequence Your Genes—And Help You Sell Them to Science*, WIRED (Dec. 15, 2016, 8:00 AM), https://www.wired.com/2016/12/genos-will-sequence-genes-help-sell-science/ [https://perma.cc/BB2W-CTTL].

101. *Id*.

102. Previously, 23andMe's research endeavors were branded under the title "Research Revolution," and subsequently was renamed "23andWe." *See* Angela L. Morrison, Note, *A Research Revolution: Genetic Testing Consumers Become Research (and Privacy) Guinea Pigs*, 9 J. TELECOMM. & HIGH TECH. L. 573, 581 n.44 (2011).

103. *Research Consent Document*, 23ANDME, https://www.23andme.com/about /consent/ [https://perma.cc/5JX4-FWVA] (last visited Aug. 19, 2018) [hereinafter *Research Consent Document*].

104. *Id*.

105. *Id*.

benefits are indirect, such as contributing to "scientific knowledge" or the development of "new drugs or tests."[106] Although compensation is not considered to be a benefit of human subjects research,[107] the consent discloses that some specific efforts may be compensated.[108] The disclosed risks of participation include: (1) theft of the customer's genetic and personal information in the event of a security breach; and (2) the possibility that a third party who has obtained some of the individual's genetic information may be able to compare that information to the anonymized genetic data published by 23andMe to reidentify the customer.[109] Although customers are not required to register with 23andMe Research in order to access the company's services, more than eighty percent of the company's customers agree to participate in research.[110]

23andMe employs certain safeguards to protect the privacy of the participants, including limiting the types of data to which the researchers have access and only publishing data that is "pooled across multiple customers" or data that includes "only very limited, non-identifying information of a single individual."[111] 23andMe's Privacy Policy states that the company reserves the right to share its customers' genetic and self-reported information "with research partners, including commercial partners."[112] The

106. *Id*.

107. OFFICE FOR HUMAN RESEARCH PROTS., *OHRP Revises its Response to the Question "When Does Compensating Subjects Undermine Informed Consent or Parental Permission?"*, U.S. DEP'T OF HEALTH & HUMAN SERVS. (Sept. 23, 2013), https://www.hhs.gov/ohrp/news/announcements-and-news-releases/2013/ohrp-revises-its-response-to-the-question-when-does-compensating-subjects-undermine-informed-consent-or-parental-permission/index.html [https://perma.cc/R8NF-4SXY] ("IRBs should not consider remuneration as a way of offsetting risks.").

108. *Research Consent Document*, *supra* note 103.

109. *Id*.

110. *23andMe Announces Agreement with Pfizer Inc. to Research Genetics of Ulcerative Colitis and Crohn's Disease*, 23ANDME (Aug. 12, 2014), https://mediacenter.23andme.com/press-releases/23andme-announces-agreement-with-pfizer-inc-to-research-genetics-of-ulcerative-colitis-and-crohns-disease/ [https://perma.cc/EJ9X-UGCE].

111. *Research Consent Document*, *supra* note 103. However, in November 2017, New York Senator Chuck Schumer called for increased scrutiny of 23andMe and other similar testing services by the Federal Trade Commission, expressing concerns about unclear privacy policies. *See* Press Release, U.S. Sen. Chuck Schumer, *Schumer Reveals: Popular at Home DNA Test Kits Are Putting Consumer Privacy at Great Risk* (Nov. 26, 2017), https://www.schumer.senate.gov/newsroom/press-releases/schumer-reveals-popular-at-home-dna-test-kits-are-putting-consumer-privacy-at-great-risk-as-dna-firms-could-sell-your-most-personal-info-and-genetic-data-to-all-comers-senator-pushes-feds-to-investigate_ensure-fair-privacy-standards-for-all-dna-kits [https://perma.cc/4KZ3-Y5EL]; Offord, *supra* note 85.

112. *Terms of Service*, 23ANDME, https://www.23andme.com/about/tos/ [https://perma.cc/9ZTH-98LP] (last visited Aug. 19, 2018). "Aggregate" information is that

company claims that, when collaborating with academic researchers, customers' raw data "never leaves the company without [their] explicit consent."[113] In cases in which an individual consents to research but changes her mind, she may withdraw consent to future research. In other words, her genetic information will be withdrawn from future studies, but any prior research performed with the data "will not be reversed, undone, or withdrawn."[114]

Another personal genetic testing company, Color Genomics, also uses its customers' "de-identified sample[s], genetic information, [personal and family health information], and [r]esults" in research performed in-house and with third-party collaborators.[115] In contrast to 23andMe's "opt in" approach, Color Genomics' Privacy Policy states that customers "can opt out of such third party research . . . by updating [their] account settings or by notifying the healthcare provider who ordered [their] [t]est."[116] Upon agreement to participate in research, Color anonymizes information and "make[s] it accessible and searchable in [a] database by researchers and the general public, for an indefinite period of time."[117]

Where shared information does not include identifiable personal information, such as data that has been de-identified or anonymized, many companies do not seek consent from their customers. For example, Color Genomics also states in its Privacy Policy that it may de-identify and aggregate genetic information that it obtained by providing genetic-analysis services, and submit that information "to public databases like ClinVar to advance

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which "has been combined with that of other users and analyzed or evaluated as a whole, such that no specific individual may be reasonably identified," while "pseudonymized" information is that which has been stripped of any identifying data so that a customer "cannot reasonably be identified as an individual." *Privacy Highlights, supra* note 75.

113. Offord, *supra* note 85.

114. *Research Consent Document*, *supra* note 103.

115. *Color Privacy Policy*, COLOR, https://www.color.com/privacy-policy [https://perma.cc/NS33-XVR] (last updated May 25, 2018) [hereinafter *Color Privacy Policy*].

116. *Color Informed Consent for the BRCA Test, the Hereditary Cancer Test, the Breast & Ovarian Cancer Test, and the Hereditary High Cholesterol Test*, COLOR, https://www.color.com/informed-consent [https://perma.cc/LZH5-QY3G] (last updated May 1, 2018) ("Color may engage in research with such third parties to develop new tests and inventions, or to validate and improve existing technologies or processes. You acknowledge and understand that Color may receive financial compensation to conduct such research, which may include providing your de-identified data to such third parties.").

117. *Id*. The Consent continues, explaining that "[p]articipation in this database involves the possible risk that your information might become known to individuals outside of Color, or that you may be identifiable from information in the database." *Id*.

medical research."[118] Similarly, by purchasing Helix's services, a customer is notified that Helix "may publicly share descriptive statistics about Aggregated Genetic Information, de-identified and aggregated Self-Reported and usage of our Services."[119] Many companies, like Genos, use aggregated genetic information to conduct internal "research or population studies," which may be published and shared with other researchers, or the public at large.[120]

B. Informed Consent to Storage and Retention of Biological Samples

The personal information that genetic testing companies may collect and use for research purposes is not limited to the genetic information that is extracted as part of their services and stored as electronic data. It is not uncommon for direct-to-consumer genetic testing companies to retain their customers' physical biospecimens for research purposes as well.

The consent practices for the storage and use of biospecimens closely mirrors practices for the use of genetic information. In 23andMe's Parkinson's disease research protocol, participants consent to the storage and use of their samples by both 23andMe and Genentech.[121] Generally, 23andMe customers have the option of filling out a Biobanking Consent Document, which allows 23andMe to store an individual's biospecimen for undefined future research purposes.[122] Receiving consent to biobank an individual's biospecimen allows "23andMe and its contractors [to] access and analyze [the individual's] stored sample, using the same or more advanced technologies," as permitted by its Terms of Service and Privacy Policy.[123] Even if a 23andMe customer does not consent to biobanking, his sample may still be preserved according to the general privacy policy "subject to the laboratory's legal and

118. *Color Privacy Policy*, *supra* note 115.

119. *Helix Privacy Policy*, HELIX, https://www.helix.com/privacy [https://perma.cc/U66H-F5L9] (last modified July 27, 2018).

120. *Privacy Policy*, GENOS, https://genos.co/privacy.html [https://perma.cc/D8KF-SSZX] (last modified July 31, 2017).

121. *See* Antonio Regalado, *23andMe's New Formula: Patient Consent = $*, MIT TECH. REV. (Jan. 6, 2015), https://www.technologyreview.com/s/534006/23andmes-new-formula-patient-consent/ [https://perma.cc/LZ3W-GL4N].

122. *Biobanking Consent Document*, 23ANDME, https://www.23andme.com/about/biobanking/ [https://perma.cc/NSS5-B6WX] (last visited Aug. 18, 2018).

123. *Id*.

regulatory requirements."[124] Other companies, such as Color Genomics, retain a blanket right in their general privacy policies to "disclose [customer] information when [they] believe in good faith that doing so is appropriate or necessary in order to enforce [their] Terms of Service."[125]

IV. REGULATION OF RESEARCH UTILIZING BIOSPECIMENS AND DATA COLLECTED FROM DIRECT-TO-CONSUMER GENETIC TESTING SERVICES

A. The Original Common Rule

Initially adopted in 1991, the Common Rule—the regulations governing human subject research in the United States for research conducted or supported by any of fifteen federal departments or—sought to put the Belmont Report principles of respect for persons, beneficence (including its corollary, nonmaleficence), and justice into practice.[126] Respect for persons includes (1) respect for autonomous decision-making for those capable of it and (2) protection for those with diminished autonomy.[127] It is accomplished mainly by ensuring voluntary participation through informed consent.[128] The Common Rule defines research as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."[129] It requires that

124. *Privacy Highlights*, *supra* note 75.

125. *Color Privacy Policy*, *supra* note 115.

126. OFFICE FOR HUMAN RESEARCH PROTS., *Federal Policy for the Protection of Human Subjects ('Common Rule')*, U.S. DEP'T HEALTH & HUMAN. SERVS. (Mar. 18, 2016), https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html [https://perma.cc/M78C-3QUP]; *see* Shawn Kennedy, *The National Research Act—1974*, IMARC RESEARCH (May 19, 2015), http://www.imarcresearch.com/blog/the-national-research-act-1974 [https://perma.cc/E5TQ-GKQM] (listing the three guiding principles of the Belmont Report). In 1974, Congress passed the National Research Act, which created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Kennedy, *supra*. The National Commission's report, also known as the Belmont Report, is the major governing document for the ethical conduct of human-subjects research in the United States. OFFICE FOR HUMAN RESEARCH PROTS., *supra*.

127. DEP'T OF HEALTH, EDUC., & WELFARE, NAT'L COMM'N FOR THE PROT. OF HUMAN SUBJECTS OF BIOMEDICAL & BEHAVIORAL RESEARCH, PUB. NO. (OS) 78-0012, THE BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH 4–5 (1979) [hereinafter DEP'T OF HEALTH, EDUC., & WELFARE, NAT'L COMM'N].

128. *See* 45 C.F.R. § 46.116 (2017); *see also* DEP'T OF HEALTH, EDUC. & WELFARE, NAT'L COMM'N, *supra* note 127, at 10.

129. 45 C.F.R. § 46.102(d) (2017).

investigators explain to participants the purposes of their research, the mechanisms in place to ensure confidentiality, and the risks of the research.[130]

The 1991 Common Rule (the "original Common Rule") applies to "all research involving human subjects" that is "subject to regulation by any federal department or agency" that has adopted the Rule.[131] To clarify whether research involves "human subjects," the Common Rule defines "human subjects" to include individuals about whom an investigator obtains "[d]ata through intervention or interaction with the individual" or "[i]dentifiable private information."[132] This limited definition made it unclear whether research utilizing biospecimens or genetic information constitutes human subjects research that is subject to the Common Rule.

The original Common Rule also includes several exemptions from IRB oversight and informed consent for research not deemed to be "human subjects" research. One such exemption in the original Rule was for "[r]esearch involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens" if they are "publicly available" or if the investigator records the information "in such a manner that subjects cannot be identified."[133]

In 2010, 23andMe published its first genome-wide association study in *PLoS Genetics*.[134] Publication of the company's article in the open-access, peer-reviewed journal was delayed for six months to allow for a more thorough investigation of a number of issues, including participant consent.[135] At first, the submission was flagged for failing to provide proof that the study had been approved by an IRB,[136] which is a requirement for any human subjects research published by *PLoS*.[137] However, after the initial

130. *Id.* § 46.116.

131. *Id.* § 46.101.

132. *Id.* § 46.102(f).

133. *Id.* § 46.101(b)(4).

134. Greg Gibson & Gregory P. Copenhaver, Editorial, *Consent and Internet-Enabled Human Genomics*, PLOS GENETICS, June 2010, at 1, http://journals.plos.org/plosgenetics/article/file?id=10.1371/journal.pgen.1000965&type=printable [https://perma.cc/VT8D-UQNY].

135. *Id*.

136. *Id*.

137. *Human Subjects Research*, PLOS GENETICS, http://journals.plos.org/plosgenetics/s/human-subjects-research [https://perma.cc/9E46-Q8LY] (last visited Aug. 18, 2018).

round of review, 23andMe secured an exemption from full review through an independent IRB on the basis that its activities were not "human subjects research."[138] This decision seemed to reflect the Office for Human Research Protections (OHRP)'s understanding of research involving private information or biospecimens in the 2010s. A 2008 OHRP guidance had suggested that studies using samples that were not collected for the purpose of research "through an interaction or intervention with living individuals," and for which "the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain," do not constitute human subjects research.[139]

In an editorial published alongside 23andMe's article, the *PLoS* editors suggested that this "unfortunate loophole" validated the company's consent procedures.[140] The consent document employed by 23andMe at the time explained the services offered by the company, the risks of "obtaining unanticipated self-knowledge," and that the samples would "be used to advance the field of genetics and human health."[141] The company also promised to obtain additional consent before sharing any individual-level data with other investigators or organizations.[142] The editors found a number of concerns with the form, including "the use of technical jargon in the document that may limit understanding, ambiguity over what data participants understand will be published, and whether standard legal requirements are met by the document."[143] Although the editors ultimately concluded that the document met the minimal legal requirements, they explained that a formal IRB review would have likely led to a more effective consent process and expounded on the need for more standardized processes and procedures for consent in human genomic

138. Gibson & Copenhaver, *supra* note 134, at 2.

139. OFFICE FOR HUMAN RES. PROTS., U.S. DEP'T OF HEALTH & HUMAN SERVS., CODED PRIVATE INFORMATION OF SPECIMENS USE IN RESEARCH, GUIDANCE (2008); *see also* Human Subjects Research Protections, 76 Fed. Reg. 44512, 44519 (proposed July 26, 2011) (to be codified at 45 C.F.R. pts. 46, 160, & 164) (acknowledging that "the current rules . . . allow research without consent when a biospecimen is used for research under conditions where the researcher does not possess information that would allow them to identify the person whose biospecimen is being studied").

140. Gibson & Copenhaver, *supra* note 134, at 2.

141. *Id*.

142. *Id*.

143. *Id*.

research.[144]

As this experience illustrates, under the original iteration of the Common Rule, the question of whether research utilizing biospecimens collected as part of a direct-to-consumer commercial service constitutes human subjects research remained unsettled.[145]

In 2013, the Office of the Inspector General of the Department of Health and Human Services issued guidance explaining that research using biospecimens that are labeled with personally identifying information (PII) is human subjects research.[146] It acknowledged that those conducting biospecimen research could utilize various models of informed consent, including tiered consent and broad consent. The guidance differentiated between the two, stating that "[t]iered consent includes options for subjects to decline inclusion of their biospecimens in specific types of future research. The broad consent model simply asks subjects to consent to all future research."[147]

A second avenue that has been suggested to exempt personal genetic testing companies' research activities from Common Rule oversight is an exemption in the original Common Rule for "survey procedures."[148] Survey procedures are exempt from the Common Rule unless the information is recorded in such a manner that the subjects are directly or indirectly identifiable, and the information is of such a nature that disclosing it to the public could place the subjects at risk of liability or be damaging to their "financial standing, employability, or reputation."[149] However, the contribution of biological samples and genetic information goes beyond simple survey procedures, and the revelation of personal behavioral and physical information as well as family history could easily affect employability and reputation.

Regardless of whether the research being performed falls into

144. *Id*.

145. *See* Christian M. Simon et al., *Active Choice But Not Too Active: Public Perspectives on Biobank Consent Models*, 13 GENETICS MED. 821, 821 (2011); Katherine Wasson, *Direct-to-Consumer Genomics and Research Ethics: Should a More Robust Informed Consent Process Be Included?*, AM. J. BIOETHICS, June–July 2009, at 56–57.

146. STUART WRIGHT, OFFICE OF INSPECTOR GEN., DEP'T OF HEALTH & HUMAN SERVS., OEI-01-11-00520, BIOSPECIMEN RESEARCH: MEETING BASIC HUMAN SUBJECTS PROTECTION REQUIREMENTS AND COMMUNICATING INFORMATIONAL RISKS 1 (2013).

147. *Id*. at 3.

148. *See* Koch, *supra* note 8, at 57.

149. 45 C.F.R. § 46.101(b)(2) (2017).

one of the Common Rule's enumerated categories of exempt research, direct-to-consumer genetic testing companies are not covered by the Common Rule if the research does not utilize any federal funds.[150] If a company intends to bring a product to market, however, the research may be subject to the Food and Drug Administration's (FDA) human subject protection requirements, which are similar to those enumerated in the Common Rule.[151] FDA regulations govern clinical studies submitted in marketing applications for new drugs, biological products, and medical devices.[152] Under FDA rules, there are eight basic elements of informed consent, including an explanation of the purposes of the research and the expected duration of participation, a description of the procedures to be followed, identification of any experimental procedures, a description of foreseeable risk, appropriate alternative procedures or courses of treatment, and a statement of voluntariness.[153]

Importantly, certain studies may not be subject to FDA oversight, as the agency's authority only covers trials relied upon to determine and establish a product's safety and efficacy[154]—not, for example, studies necessary for obtaining patent protections, Phase IV trials, or trials where the company and/or sponsor are seeking to identify genetic predispositions to traits or illnesses, but are not seeking to create a drug or device that would require FDA approval.[155]

B. The Revised Common Rule and Research Involving Biospecimens

For the first time in two decades, in 2011, the United States Department of Health and Human Services (HHS) began contemplating major changes to the Common Rule.[156] It released

150. *See* 45 C.F.R. § 46.101(a) (2017); *Id.* § 46.122.

151. *See* 21 C.F.R. § 50.1(a) (2018); *Id.* § 56.101(a); *Id.* § 312.1(a); *Id.* § 812.1(a); *Comparison of FDA and HHS Human Subject Protection Regulations*, FDA (Apr. 3, 2018), https://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/EducationalMaterials/ucm112910.htm [https://perma.cc/7MVB-3RCX] [hereinafter *Comparison of FDA and HHS Human Subject Protection Regulations*].

152. *See Comparison of FDA and HHS Human Subject Protection Regulations*, *supra* note 151.

153. 21 C.F.R. § 50.25 (2018).

154. *See* 21 C.F.R. § 54.2(e) (2018).

155. *See* U.S. GOV'T ACCOUNTABILITY OFFICE, GAO-06-402, DRUG SAFETY: IMPROVEMENT NEEDED IN FDA'S POSTMARKET DECISION-MAKING AND OVERSIGHT PROCESS 6 (2006) (discussing FDA's role in determining drug safety).

156. *See* Human Subjects Research Protections, 76 Fed. Reg. 44512, 44519 (proposed July 26, 2011) (to be codified at 45 C.F.R. pts. 46, 160, & 164).

an Advance Notice of Proposed Rule Making (ANPRM) in 2011, which suggested, among other things, the modification and streamlining of informed consent forms, implementation of a risk-based review process, standardization of data security measures, expansion of the jurisdiction of the Common Rule to govern all studies conducted in institutions that receive federal funding, and centralized IRB review.[157] Four years later, after significant notice, comment, and revisions, HHS released its Notice of Proposed Rulemaking (NPRM).[158] Finally, on January 19, 2017, President Obama's last day in office, it released the final revisions to the Common Rule (the "final Rule" or the "revised Common Rule").[159] Although the final Rule was scheduled to take effect on January 19, 2018, on January 17, 2018, implementation of the revisions was delayed for six months.[160] In June 2018, implementation was again delayed until January 2019.[161]

1. The Definition of Human Subjects.

In response to the evolving nature of biospecimen research and concerns about the possibility of re-identification of previously de-identified biospecimens collected for genomic studies,[162] regulators began considering revising the Common Rule to address whether research utilizing collected biospecimens constitutes human subjects research. The revised Common Rule expands and clarifies the extent to which biological specimens are considered "human subjects" for the purposes of the Common Rule. In its 2011 ANPRM, HHS proposed to extend coverage of the Common Rule's requirements to non-identifiable biospecimens.[163]

157. *Id*. at 44519–44528.

158. Federal Policy for the Protection of Human Subjects, 80 Fed. Reg. 53933 (proposed Sept. 8, 2015) (to be codified at 45 C.F.R. pt. 46).

159. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149 (proposed Jan. 19, 2017) (to be codified at 45 C.F.R. pt. 46).

160. Federal Policy for the Protection of Human Subjects: Delay of the Revisions to the Federal Policy for the Protection of Human Subjects, 83 Fed. Reg. 2885, 2886–87 (proposed Jan. 22, 2018) (to be codified at 45 C.F.R. pt. 46). The delay was intended to provide "institutions more time to prepare to implement the provisions of the revised Common Rule." *Delay of the Revised Common Rule: What Does it Mean for Me?*, PRIM&R (Jan. 18, 2018), https://www.primr.org/commonrule/resources/DelayWhatDoesItMean [https://perma.cc/AVE3-92RP].

161. Federal Policy for the Protection of Human Subjects: Six Month Delay of the General Compliance Date of Revisions While Allowing the Use of Three Burden-Reducing Provisions During the Delay Period, 83 Fed. Reg. 28497 (proposed June 19, 2018) (to be codified at 45 C.F.R. pt. 46).

162. Melissa Gymrek et al., *Identifying Personal Genomes by Surname Inference*, 339 SCIENCE 321, 321 (2013).

163. *See* Human Subjects Research Protections, 76 Fed. Reg. 44512, 44525 (proposed July 26, 2011) (to be codified at 45 C.F.R. pts. 46, 160, & 164).

However, revisions defining "human subjects" research to include all biospecimens, regardless of identifiability, were ultimately left out of the final Rule due to concerns that doing so would unnecessarily hinder research by overwhelming researchers with excessive administrative duties.[164]

Thus, the final Rule does not expand the definition of "human subject" to include non-identified biospecimens. It defines human subjects research as that which utilizes "information or biospecimens" that are obtained through "intervention or interaction" and that will be "use[d], studie[d], or analyze[d]."[165] Thus, if the specimen or data is collected for a particular study, it is subject to the revised Common Rule. In addition, when an investigator "[o]btains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens," the research is subject to the final Rule, even if the information or biospecimens had been previously collected for clinical purposes or for another study.[166] Thus, research using non-identifiable biospecimens previously collected for another purpose will not be classified as human subjects research—and therefore consent would not be required for their use in future research protocols—but research with identifiable biospecimens will be subject to the requirements of the revised Common Rule.

Similar to the original Common Rule, the revised Rule also identifies a number of activities falling under the umbrella of research that are exempt from the Common Rule's coverage. Under the revised Rule, secondary research for which consent is not required is exempt when the identifiable information or biospecimens are publicly available; when the information is recorded in such a way that it cannot readily be identified and the investigator does not contact the subjects or re-identify the information; when the information is analyzed for the purposes of "health care operations," "research," or "public health activities"; and when the information was collected by the government for

164. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149, 7165 (proposed Jan. 19, 2017) ("The reasons for opposing the expansion of the definition of 'human subject' to include all biospecimens were numerous, including: the feasibility of obtaining broad consent in a clinical setting; the costs of obtaining, tagging, and tracking consents given the low risk nature of the research in question; allowing autonomy to trump beneficence and justice; insufficient evidence of risk or public concern about the issue; the fact that it would result in fewer specimens collected from fewer sources, with adverse implications for rare diseases and for justice; the idea that requiring all biospecimens to remain identified poses greater privacy and confidentiality risks than the current system; and overall negative impacts on research.").

165. *Id*. at 7260.

166. *Id*.

non-research purposes and will be stored according to standards set by the Privacy Act of 1974.[167]

The revised Common Rule also attempts to provide greater clarity regarding when a biospecimen is deemed to be identifiable.[168] The original iteration of the Common Rule provides an umbrella definition of identifiable information that included any private information for which "the identity of the subject is or may readily be ascertained by the investigator or associated with the information."[169] However, the revised Common Rule recognizes that the technology that could be utilized to render a previously unidentifiable biospecimen re-identified is changing rapidly.[170] Thus, the final Rule instructs all agencies, within a year of implementing the revised Rule and then every four years after, to reexamine the definition of "identifiable" and—if necessary and in compliance with applicable law—change their definition of the term.[171] They must also assess which, if any, technologies or techniques create per se identifiable information.[172]

2. Limited IRB Review Required for the Storage or Maintenance of Biospecimens.

Also exempt from the revised Common Rule is the storage or maintenance of identifiable information and biospecimens that have passed a limited IRB review.[173] The revised Common Rule establishes three criteria that must be met in order for such an activity to pass a limited review. First, the IRB must establish that broad consent for the "storage, maintenance, and secondary research use" of identifiable biospecimens was properly obtained.[174] The IRB must then establish that the consent or waiver was appropriately documented.[175] Finally, the IRB must find that there are appropriate provisions in place to protect the privacy of the information if a change has been made in the way the data is stored or maintained.[176]

167. *Id*. at 7262.
168. *Id*. at 7169.
169. 45 C.F.R. § 46.102(f)(2) (2017).
170. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. at 7169.
171. *Id*.
172. *Id*.
173. *Id*. at 7262–63.
174. *Id*. at 7264.
175. *Id*.
176. *Id*.

3. Informed Consent.

The revised Common Rule aims to address the modern research climate by requiring certain disclosures as part of the informed consent process. Under the final Rule, if the research involves the collection of identifiable biospecimens, the consent form must include either a statement indicating that the identifying aspects of that data may be removed and that the information may be used for future research studies or distributed to another investigator, or a statement that even the participant's non-identified data will not be shared.[177] Further disclosures concerning whether the biospecimens may be used for commercial profit and whether the research may involve whole genome sequencing may also be required.[178]

i. Broad Consent. To acknowledge the modern practice of collecting biospecimens for unrelated (research or clinical) purposes that are then used for future research endeavors, the revised Common Rule created a new provision explicitly outlining the process by which an institution can procure broad consent (rather than study-specific consent) for secondary research on identifiable specimens. When researchers obtain broad consent under the revised Rule for the "storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens," future research is exempt from formal informed consent requirements, and the study requires only limited IRB review.[179]

To obtain broad consent, the revised Rule requires researchers to provide a general description of the types of research that may be performed using the identifiable information or biospecimens, as well as the type of information that may be used, whom that information might be shared with, and the manner and length of time for which the identifiable information and biospecimens may be stored and maintained.[180] Finally, the broad consent form must disclose whether the subject will be informed of the details of any future studies, and that the individual may—or may not—be informed of any clinically

177. *Id*. at 7266.

178. *Id*.

179. *See* SEC'Y ADVISORY COMM. ON HUMAN RESEARCH PROTS., OFFICE FOR HUMAN RESEARCH PROTS., U.S. DEP'T OF HEALTH & HUMAN SERVS., ATTACHMENT C—RECOMMENDATIONS FOR BROAD CONSENT GUIDANCE (2017), https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-august-2-2017/index.html [https://perma.cc/ADS2-WHT7].

180. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. at 7266.

relevant results.[181] Under the revised Rule, an IRB also may not omit or alter any of the broad consent-specific elements.[182]

ii. Waiver of Consent. To address the proliferation of stored, identifiable data being used in modern research, the revised Common Rule includes an additional criterion that is meant to "protect the privacy of individuals" without "unduly inhibiting research."[183] In order to qualify for a consent waiver for research with identifiable biospecimens, the revised Rule requires an added finding that "the research could not practicably be carried out without the waiver" and that the donors had not originally refused to provide their broad consent to research.[184] This change protects individual privacy by encouraging, whenever possible, non-identifiable data to be used.[185]

Further, the final Rule adopts a new waiver provision meant to facilitate activities relating to "screening, recruiting, or determining the eligibility of prospective subjects."[186] Under the original Common Rule, researchers are required to either meet the traditional criteria to waive consent or obtain consent for minimally invasive activities.[187] However, the new provision allows an IRB to waive the requirement of informed consent when researchers "will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects" if either the information is obtained through oral or written communication with the subject, or the investigator will be using stored records or biospecimens.[188] This provision was meant to reduce the burden associated with meeting the traditional waiver requirement, which critics considered unnecessary for protecting privacy in such situations.[189]

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181. *Id*. at 7266–67.

182. *Id*. at 7267.

183. *Id*. at 7225–26.

184. *Id*. at 7267; *see also* Holly Fernandez Lynch, *A New Day for Oversight of Human Subjects Research*, HEALTH AFF. BLOG (Feb. 6, 2017), https://www.healthaffairs.org/do/10.1377/hblog20170206.058637/full/ [https://perma.cc/R8MJ-LL9A] ("[T]he new rule will now require only an added finding that research would not be practicable with nonidentified specimens and that specimen sources have not declined to provide their broad consent to research.").

185. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149, 7224 (proposed Jan. 19, 2017) (to be codified at 45 C.F.R. pt. 46).

186. *Id*. at 7267.

187. *Id*. at 7224.

188. *Id*. at 7267.

189. *Id*. at 7227.

4. Summary of Revised Common Rule Requirements for Research with Biospecimens.

When biospecimens are collected—either for research or clinical purposes—and researchers seek to use those specimens or data for other purposes, the revised Common Rule maintains the previous understanding that non-identifiable specimens do not qualify as human subjects research, and therefore IRB oversight and informed consent are unnecessary. When the biospecimens or data are identifiable, they are subject either to IRB oversight and informed consent requirements or can qualify for an exemption. Under standard Common Rule IRB requirements, researchers may seek study-specific consent or seek a consent waiver.[190] If researchers seek and qualify for an exemption from the Common Rule's requirements for IRB review for research utilizing identifiable biospecimens or data, regulators may either require limited IRB review and broad consent, or regulators may not require consent at all.[191]

5. Provisions Not Incorporated into the Final Rule.

The revised Common Rule excludes a few major proposals from the 2011 ANPRM and the 2015 NPRM. One of the most controversial changes proposed by the NPRM suggested expanding the Common Rule to define all research involving biospecimens, regardless of identifiability, as human subjects research.[192] The provision was included to address a growing concern that biospecimen donors had little to no control over how their specimens were used.[193] Advances in the field have made it easier than ever before to extract significant amounts of information from biospecimens, including DNA, which researchers

190. *Id*. at 7219.

191. Lynch, *supra* note 184. Such research is exempt and does not require consent when the information is publicly available; is recorded in a way that the identity of the subject cannot readily be ascertained and the investigator does not contact or re-identify subjects; is identifiable health information regulated under HIPAA used for "healthcare operations" or "public health activities"; or is research "conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information" and maintained in compliance with applicable laws/privacy protections. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. at 7261–62.

192. Federal Policy for the Protection of Human Subjects, 80 Fed. Reg. 53933, 54004 (proposed Sept. 8, 2015) (to be codified at 45 C.F.R. pt. 46).

193. *See* Thomas D. Shrack et al., *Proposed Revisions to the Common Rule Receive Harsh Criticism from Industry Stakeholders*, LEXOLOGY (Dec. 22, 2015), http://www.lexology.com/library/detail.aspx?g=2a59a3ee-c9ee-40d4-91a4-b7b5d698d76c [https://perma.cc/FNZ8-L48W] ("The NPRM took the position that secondary use without consent should be prohibited because research subjects should have control over the circumstances in which personal information can be derived from their specimens.").

can de-identify and use for research that is unrelated to the activity for which the donor provided consent.[194] Although the proposal might have empowered individual donors, it faced pushback by about ninety-five percent of the patients and members of the research community who provided comments on the NPRM.[195] Critics suggested that incorporating this provision into the final Rule would disparately prioritize individual autonomy at the expense of promoting "beneficence and justice," and be unduly expensive and complex to implement.[196]

A second significant proposed change that was not incorporated into the final Rule would have expanded the scope of the Common Rule beyond research that is supported by federal funding or is subject to a federal-wide assurance (FWA).[197] The proposed change would have required that all research performed at institutions receiving any support from a Common Rule department or agency comply with the policy, regardless of the source funding the specific study.[198] Therefore, any human subjects research performed by a private direct-to-consumer genetic testing company that is privately funded would have been subject to Common Rule regulations if the company received federal funding for any other human subjects research. The proposal faced criticism for unnecessarily adding to research institutions' administrative burdens, covering minimal-risk research activities, and for being unduly complex to implement.[199]

V. APPLICATION OF THE REVISED COMMON RULE TO RESEARCH CONDUCTED BY DTC GENETIC TESTING COMPANIES AND THEIR PARTNERS

Although the majority of studies that use genetic information collected by direct-to-consumer genetic companies are currently privately funded, more federally-funded studies have been initiated in recent years, as shown by the studies mentioned below.

194. *See id.* ("Biospecimens are often used for continued research unrelated to the purpose for which they were originally collected (a 'secondary use'), and it is often possible to extract DNA from biospecimens to obtain individually identifiable data.").

195. COUNCIL ON GOVERNMENTAL REL., ANALYSIS OF PUBLIC COMMENTS ON THE COMMON RULE NPRM 1–2 (2016), https://www.cogr.edu/sites/default/files/Analysis%20of%20Common%20Rule%20Comments.pdf [https://perma.cc/3AM6-6HDJ].

196. Shrack et al., *supra* note 193.

197. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149, 7154–55 (Jan. 19, 2017) (to be codified at 45 C.F.R. pt. 46).

198. *See* Federal Policy for the Protection of Human Subjects, 80 Fed. Reg. 53933, 54045 (proposed Sept. 8, 2015) (to be codified at 45 C.F.R. pt. 46).

199. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. at 7155–56.

Under such circumstances, researchers are required to follow the Common Rule for federally-funded studies that are performed by either the company or a third party using their data. In 2014, the National Institutes of Health awarded 23andMe a 1.4 million dollar grant to support its work in identifying rare genetic variants for diseases, and to allow external researchers access to 23andMe's vast genetic databases.[200] The partnership was renewed two years later by the NIH's National Human Genome Research Institute.[201] The 2016 grant, worth 1.7 million dollars, aims to reduce disparities in genetic research by creating a large-scale genetic sequencing panel of African American participants.[202] As more direct-to-consumer genetic testing companies begin explicitly conducting their own research or partnering with other research entities, more federal funding is likely to follow, and more companies will be subject to the requirements of the Common Rule.

Moreover, some direct-to-consumer genetic testing companies may choose to voluntarily abide by the revised Common Rule. Among the larger companies, 23andMe became the first to follow the regulations by voluntarily applying it to all of their internal research.[203] While some companies may choose to do so due to a perceived ethical obligation to "treat[] people right in research,"[204] others may elect to follow the federal standards in order to temper negative publicity relating to recent concerns about customer privacy and transparency.[205]

However, not all companies follow—voluntarily or otherwise—the Common Rule's requirements for safe and ethical human subjects research. Based on a review of four companies' websites, one study concluded that the DTC genetic testing

200. *23andMe Scientists Receive Approximately $1.4 Million in Funding from the National Institutes of Health*, 23ANDME (July 29, 2014), https://mediacenter.23andme.com/press-releases/nih_grant_2014/ [https://perma.cc/SY3K-EFTU].

201. *23andMe, NIH Work to Reduce Health Research Disparities Among African Americans*, 23ANDME (Oct. 13, 2016), https://mediacenter.23andme.com/press-releases/23andme-nih-work-to-reduce-health-research-disparities-among-african-americans/ [https://perma.cc/S3HQ-FTFD].

202. *Id*.

203. *Protecting People in People Powered Research*, 23ANDMEBLOG (July 30, 2014), https://blog.23andme.com/23andme-research/protecting-people-in-people-powered-research/ [https://perma.cc/6TDK-YUNJ].

204. *Id*.

205. *See, e.g.*, *Curious About Your Genes? Companies Standing to Profit are Too!*, BLOOMBERG (May 23, 2017), https://www.bna.com/curious-genes-companies-b73014451420/ [https://perma.cc/AV4K-KUXG]; Dan MacGuill, *Can Ancestry.com Take Ownership of Your DNA Data?*, SNOPES (May 23, 2017), http://www.snopes.com/ancestry-dna-steal-own/ [https://perma.cc/YVJ3-U4XQ].

companies' "unclear and non-explicit way of 'recruiting' consumers as research participants appears to be in contradiction of the requirement for informed consent."[206]

A. Informed Consent Disclosures

Overall, there is a general trend among personal genetic testing companies to reserve, as part of their basic services, a right to use their customer's anonymized, aggregated data for undefined research purposes.[207] However, the majority of personal genetic testing companies' consent forms do not provide the potential customer with any information on where or to whom their genetic information will be disclosed, or what types of research their biospecimens or data may be used for in the future.[208] And it appears some companies do not allow a customer to opt out of their research efforts.[209]

Current behavior by direct-to-consumer genetic testing companies raises a number of issues regarding informed consent, the first of which is a failure to adequately disclose the potential future uses of collected biospecimens for storage and research.

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206. Emilia Niemiec & Heidi Carmen Howard, *Ethical Issues in Consumer Genome Sequencing: Use of Consumers' Samples and Data*, APPLIED & TRANSLATIONAL GENOMICS, Mar. 2016, at 23, 26, http://www.sciencedirect.com/science/article/pii/S2212066116300059 [https://perma.cc/4LVZ-YYZC]. Focusing on the most basic element of informed consent—the informed consent document—they continued, "[n]either of the two companies that may conduct research [GeneYouIn and Gene by Gene] and were examined here offered a separate informed consent form for research." *Id*.

207. Some companies may reserve even further rights in their basic privacy policies to the customer's identifiable information. Veritas Genetics includes a more sweeping form of consent in its Privacy Policy that grants the company the right to "use or disclose [customers'] Protected Health Information for research purposes" that have been reviewed "by a committee responsible for ensuring the protection of individual research subjects, appropriate patient authorization and an adequate plan to safeguard Protect [sic] Health Information." *Notice of Privacy Practices*, VERITAS (Apr. 1, 2015), https://www.veritasgenetics.com/sites/default/files/media/documents/Notice_of_Privacy_Practices_v0.2_brand_update.pdf[https://perma.cc/6SZC-CWLZ]. By using Pathway Genomics services, customers similarly agree that their Personal Health Information can be used "in connection with research performed by us and by researchers outside Pathway." *Pathway Genomics Corporation Notice of Privacy Practices*, PATHWAY GENOMICS (Oct. 6, 2014), https://www.pathway.com/wp-content/uploads/2017/06/PG_NoticePrivacy Practices.pdf [https://perma.cc/RN6A-FCUH]. Pathway's studies are "generally" subject to IRB review, and when law, policy, and the IRB permit, PHI can be used and disclosed without consent. *Id*.

208. *See* Kristen V. Brown, *What DNA Testing Companies' Terrifying Privacy Policies Actually Mean*, GIZMODO (Oct. 18, 2017, 10:10 AM), https://gizmodo.com/what-dna-testing-companies-terrifying-privacy-policies-1819158337 [https://perma.cc/XR5E-8T6Q].

209. *See, e.g.*, Will Simonds, *23andMyIdentity: How to Safely and Privately Take a Genetic Test*, ABINE BLOG (Feb. 11, 2016), https://www.abine.com/blog/2016/23andmyidentity-how-to-safely-and-privately-take-a-genetic-test/ [https://perma.cc/8Q9U-5KQ3] (stating 23andMe makes consenting to research necessary for the genetic testing procedure).

Peter Pitts, President of the Center for Medicine in the Public Interest and a former FDA Associate Commissioner, explained that 23andMe's customers "have to wade through pages of fine print" in order to find out that their information may be shared with research and commercial partners.[210] Recent studies have shown that genetic testing companies "frequently fail to meet even basic international transparency standards."[211] Although these companies obtain clear consent for the actual testing services, "information about data reuse for research or other purposes [is] often sparse and consent options limited or unclear."[212] This may lead to confusion among customers, especially those who believe that by not opting into an explicit research initiative, like 23andMe Research, their data will not be used for research purposes.

B. Broad Consent

Further, except for rare studies such as 23andMe's Parkinson's disease project, in which the company obtains explicit individual consent, direct-to-consumer genetic testing companies often use vague language regarding future uses of individuals' biospecimens and data, wording consent forms so as to reserve a right to the customer's data for unspecified research purposes or an unspecified amount of time.[213] According to healthcare historian Arthur Daemmrich of the Smithsonian Institute, direct-to-consumer testing companies "can't tell you today who they're going to license your data to and for what purpose."[214] Consumers may unknowingly be consenting not only for their genetic data to be used for studies to which they may have explicitly objected if given the opportunity, but for their information, and in some cases physical biospecimens, to be used far into the future.[215]

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210. Peter Pitts, *The Privacy Delusions of Genetic Testing*, FORBES (Feb. 15, 2017, 1:26 PM), https://www.forbes.com/sites/realspin/2017/02/15/the-privacy-delusions-of-genetic-testing/#6a20e3a31bba [https://perma.cc/5PQG-3MG8].

211. *Id*.

212. Jacqueline A. Hall et al., *Transparency of Genetic Testing Services for "Health, Wellness and Lifestyle": Analysis of Online Pre-Purchase Information for UK Consumers*, 25 EUR. J. HUM. GENETICS 908, 908 (2017).

213. *See* Zhang, *supra* note 97; Megan Molteni, *770,000 Tubes of Spit Help Map America's Great Migrations*, WIRED (Feb. 2, 2017, 11:00 AM), https://www.wired.com/2017/02/770000-tubes-spit-help-map-americas-great-migrations/ [https://perma.cc/U99Q-H89R].

214. Molteni, *supra* note 213.

215. *See id*. (noting direct-to-consumer companies are "'just trying to be the holder of the data'" and asking whether consent covers "'if they put samples on ice and keep them frozen forever'").

Under the original Common Rule, researchers could only use identifiable data or biospecimens for secondary research if they had obtained secondary consent, had obtained an IRB consent waiver, or had de-identified the biospecimens or data so that the Common Rule no longer applied. However, this latter approach would necessarily lead to less valuable research, in that the act of de-identification or anonymization would devalue the resource.[216]

The revised Common Rule gives direct-to-consumer genetic testing companies and their partners more options to use identifiable biospecimens or collected data. Rather than being required to seek study-specific consent for each research protocol in which these biospecimens and data are used, broad consent may be obtained, thereby obviating any obligation to obtain further consent for secondary research.

The type of consent employed by these companies reflects the move in genomic research from the traditional model of consent, where one participant agrees to participate in a specified study, to a form of broad consent where participants agree to "participate in unknown future research."[217] The ethical implications of broad versus traditional study-specific consent have been hotly debated in recent years.[218] Public comments in response to HHS' proposals to update the Common Rule were mixed on the meaningfulness of broad consent.[219] Some commentators questioned whether broad consent actually increases a participant's autonomy, while others suggested that broad consent was not consent at all, but rather "an agreement or permission."[220] Recent studies also suggest public opinion on broad consent is conflicted. One 2014 study showed that preference for broad versus traditional consent was almost evenly split.[221] Another suggests that neither broad nor traditional consent are ideal, but advocates for a more "nuanced approach" that allows participants to choose the degree of consent they wish

216. Holly Fernandez Lynch & Michelle N. Meyer, *Regulating Research with Biospecimens Under the Revised Common Rule*, 47 HASTINGS CTR. REP. 3, 3 ("Removing identifiers is not ideal because it is possible to learn more from biospecimens when they can be connected to demographic information, medical records, and other information that allows the source to be identified.").

217. Jodyn Platt et al., *Public Preferences Regarding Informed Consent Models for Participation in Population-Based Genomic Research*, 16 GENETICS IN MED. 11, 11 (2014).

218. *See generally* Mats G. Hansson et al., *Should Donors Be Allowed to Give Broad Consent to Future Biobank Research?*, 7 LANCET ONCOLOGY 266, 266–67 (2006) (discussing differing points of view of the impact of broad consent versus study-specific consent on donor autonomy and research quality).

219. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149, 7218 (proposed Jan. 19, 2017) (to be codified at 45 C.F.R. pt. 46).

220. *Id*.

221. Platt, *supra* note 217, at 13–15.

to provide.[222]

Regardless, some commentators have concluded that "researchers are unlikely to make use of the broad consent option, considering its burdens and risks."[223] Despite this prediction, broad consent may be most useful for research conducted by or in collaboration with direct-to-consumer genetic testing companies, where the biospecimens were originally collected for research purposes, particularly if the companies are able to ensure the "infrastructure that would be necessary to track a broad consent system."[224]

However, direct-to-consumer genetic testing companies could also take advantage of the final Common Rule's requirement for waiver of consent by demonstrating that the research could not practicably be conducted with non-identifiable biospecimens. Removing identifiers from the biospecimens and data collected by these companies would potentially significantly reduce their value and make the research conducted by these companies and their partners impracticable. Thus, it is likely that they would be successful in meeting the waiver criteria.

C. Re-identifiability

The various proposals to update the Common Rule attempted, in various forms, to address the oft-raised concern that de-identified (or even anonymized) biospecimens and personal data could be re-identified by enterprising individuals. Although identifying information such as name and address can be removed from genetic information so that it cannot be readily associated with an individual, whole genome sequences are unique to a single individual, and may therefore be identifiable.[225]

As technology has evolved, it has also become easier to re-identify donors using less information or fewer data points. Questions about the permanence of de-identification have increased in the last decade after a series of studies by prominent researchers demonstrated the ease of re-identification from publicly accessible information.[226] First, researchers from the

222. Flavio D'Abramo et al., *Research Participants' Perceptions and Views on Consent for Biobank Research: A Review of Empirical Data and Ethical Analysis*, 16 BIOMED. CENT. 60, 68–70 (2015).

223. Lynch & Meyer, *supra* note 216, at 3.

224. *Id*. at 3–4.

225. Spector-Bagdady, *supra* note 53, at 516.

226. Paul Ohm, *Broken Promises of Privacy: Responding to the Surprising Failure of Anonymization*, 57 UCLA L. REV. 1701, 1716 (2010).

Whitehead Institute for Biomedical Research, Baylor College of Medicine, and Tel Aviv University re-identified five "unidentified" men who had participated in the 1000 Genomes Project[227] who had also participated in a study of Mormon families in Utah, using an approach that focused on surnames and the Y chromosome.[228] Yaniv Erlich and colleagues published their study showing that it is possible to identify participants in NIH-funded public sequencing projects from de-identified genetic material using freely available genetic and demographic information.[229] The 1000 Genomes Project consent form reassured participants that re-identification would be "very hard."[230] As the Authors of the study explained, a "key feature of this technique is that it entirely relies on free, publicly accessible Internet resources."[231]

Similarly, Latanya Sweeney and colleagues re-identified participants in the Personal Genome Project (PGP), a public interest, nonprofit effort to recruit one hundred thousand participants to share their genome sequences, related health, and physical information and to regularly report their experiences.[232]

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227. The 1000 Genomes Project was established in 2008, as an international effort to sequence the genomes of approximately 2,500 people from around the world in order to create the most detailed and medically useful picture to date of human genetic variation. *About IGSR and the 1000 Genomes Project*, IGSR, http://www.1000genomes.org/about [https://perma.cc/9AFY-JWPG] (last visited Aug. 18, 2018). The collected data were available to the worldwide scientific community through freely accessible public databases. *See First Data Release: SNP Data Downloads and Genome Browser Representing Four High Coverage Individuals*, IGSR (Dec. 23, 2008), http://www.internationalgenome.org/announcements/first-data-release-snp-data-downloads-and-genome-browser-representing-four-high-covera/ [https://perma.cc/454D-8H8U] ("The first set of SNP calls representing the preliminary analysis of four genome sequences are now available to download through the EBI FTP site and the NCBI FTP site." (citations omitted)); *see also About Rare Genomics Institute*, RARE GENOMICS INST., https://www.raregenomics.org/about-us/ [https://perma.cc/9P8L-WWHE] (last visited Aug. 18, 2018). In December 2011, the National Human Genome Research Institute announced that it would give approximately $461 million to three institutes to continue work on the 1000 Genomes Project. Susan Young, *Funds Dedicated to Personalized Genetics: NIH Aims to Push Genome-Sequencing into Mainstream Medicine*, NATURE NEWS (Dec. 6, 2011), http://www.nature.com/news/funds-dedicated-to-personalized-genetics-1.9565 [https://perma.cc/FR7R-ZUH4].

228. Gymrek et al., *supra* note 162, at 323. "We show that a combination of a surname with other types of metadata, such as age and state, can be used to triangulate the identity of the target." *Id.* at 321.

229. Uduak Grace Thomas, *Not So De-Identified: Study Raises Questions About Standards for Protecting Personal Genomic Data*, GENOMEWEB (Jan. 18, 2013), https://www.genomeweb.com/informatics/not-so-de-identified-study-raises-questions-about-standards-protecting-personal [https://perma.cc/LMR8-H6AL].

230. *1000 Genomes Project: Developing a Research Resource for Studies of Human Genetic Variation*, INTERNATIONALGENOME.ORG, http://www.internationalgenome.org/sites/1000genomes.org/files/docs/Informed%20Consent%20Form%20Template.pdf [https://perma.cc/FAN7-S3BE] (last visited Aug. 18, 2018).

231. Gymrek et al., *supra* note 162, at 321.

232. LATANYA SWEENEY ET AL., IDENTIFYING PARTICIPANTS IN THE PERSONAL GENOME

The PGP is unique, in that it takes an open approach to consent, warning participants of potential re-identification and making no assurances of privacy.[233]

23andMe cofounder Linda Avey admits that "it's a fallacy to think that genomic data can be fully anonymized."[234] The phenotypic information that can be extracted from parts-or-whole-genome sequences can be cross-referenced with publicly available data, like hair or eye color, in order to identify the donor.[235] Thus, the first proposed changes to the Common Rule, in the ANPRM, "recognize[d] that there is an increasing belief that what constitutes 'identifiable' and 'de-identified' data is fluid; rapidly evolving advances in technology coupled with the increasing volume of data readily available may soon allow identification of an individual from data that is currently considered de-identified."[236] With new computational genomic techniques, genetic data can also be combined with genealogical data to create estimated genetic data for the sequenced individual's family members.[237] Privacy concerns therefore extend not just to those who are sequenced but to their family members as well.

Direct-to-consumer genetic testing companies that adhere to the Common Rule will be subject to the agencies' determinations regarding whether the meaning of "identifiable" should be changed.[238] However, there is likely to be a lag time between technological innovation and agency reassessment, and some companies may not adhere to the Common Rule's requirements at all. In such cases, consumers may be reliant on the companies' promises of de-identification, with little recourse if these promises are not honored.

VI. CONCLUSION

Although there was a general consensus that the Common

PROJECT BY NAME 1, 3 (2013), http://dataprivacylab.org/projects/pgp/1021-1.pdf [https://perma.cc/V6LM-7DQ5]; *see* Adam Tanner, *Harvard Professor Re-Identifies Anonymous Volunteers in DNA Study*, FORBES (Apr. 25, 2013, 3:47 PM), https://www.forbes.com/sites/adamtanner/2013/04/25/harvard-professor-re-identifies-anonymous-volunteers-in-dna-study/#4cd2af7792c9 [https://perma.cc/75B3-8WWK]; *see also The Personal Genome Project*, PERS. GENOME PROJECT, http://www.personalgenomes.org/us [https://perma.cc/7F2T-6E5L] (last visited Aug. 18, 2018).

233. SWEENEY ET AL., *supra* note 232, at 1–2.

234. Pitts, *supra* note 210.

235. *Id*.

236. Human Subjects Research Protections, 76 Fed. Reg. 44512, 44524 (proposed July 26, 2011) (to be codified at 45 C.F.R. pts. 46, 160, & 164).

237. Gitter, *supra* note 93, at 1292–93.

238. Lynch & Meyer, *supra* note 216, at 3–4.

Rule was due for change based on an understanding that the research enterprise had evolved significantly since its original passage in 1991, the two sets of proposals contained in the ANPRM and the NPRM were far from perfect, and the final Rule reflects an effort to accommodate researchers and research institutions while preserving participant autonomy. Health information is an inherently personal thing, and the direct-to-consumer genetic testing market offers the opportunity to further transform health information into a consumer good. Although these companies market their services as "recreational" or a customer-oriented form of entertainment and self-exploration, a large percentage of their profits are actually generated by these research efforts. The apparent de-medicalization of health information and analysis into a form of social entertainment has raised serious questions about informed consent.

The final Common Rule likely helped clarify the scope and extent to which the federal regulations apply to research conducted by direct-to-consumer genetic testing companies, and justified these companies' decisions not to seek study-specific consent, particularly where biospecimens or data has been de-identified. However, as a rule, direct-to-consumer genetic testing companies should disclose more information about their research practices in their informed consent forms in order to properly respect individuals' autonomous decision-making. Currently, companies insufficiently focus on future use of customers' biospecimens and data in future research.[239] Recognizing that the original Common Rule made it "relatively easy to use biospecimens and data for secondary research,"[240] the revised Rule does little to impose additional informed consent requirements for research conducted by direct-to-consumer genetic testing companies.

On the whole, there is little in the revised Common Rule to direct or guide direct-to-consumer genetic testing companies to ensure a more robust informed consent process for the use of customers' biospecimens and data. Despite all of their faults, the previous iterations of the proposed revisions to the Common Rule contained in the NPRM and the ANPRM endeavored to protect and respect individual autonomy in deciding whether—and when—to participate in research. In many ways, the final Rule

239. Wasson, *supra* note 145, at 57 (opining that, even under the original Common Rule, "[t]he criteria for informed consent is potentially being met at a minimal level—where consumers read information, sign a document—but could be strengthened, particularly given the complex nature of genetic results and information").

240. Lynch et al., *supra* note 54, at 4.

permits companies to continue to market themselves as proponents of the "democratization of research," despite doing little to shift research from a single-direction endeavor to a collaborative process shared by participants and researchers.[241] Not only does the status quo fail to improve the status of individual customers who find themselves to be participants in research utilizing their biospecimens and data, it also undermines public trust.

241. Koch, *supra* note 8, at 35.