The Social Life of DTC Genetics
The case of 23andMe

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The decoding of the human genome in the summer of 2002 was accompanied by the swift commodification of direct-to-consumer (or DTC) genetic tests – that is, DNA data analyses for sale to the lay public. DNA-based paternity testing had been publicly available since the early 1990s first, at select laboratories, and later through online commerce. In the late 1990s, medical genetic tests such as Myriad’s BRACAnalysis (for hereditary predisposition to breast and ovarian cancers) were introduced in clinical settings. But the subsequent decade saw a watershed of DTC genetic testing services aimed at a far broader market than potential parents and possible cancer sufferers. Readily available for purchase on the internet, these new commercial technologies targeted luxury consumers, genealogy buffs, and DIY-science geeks, among many others, and promised to tell us who we are, where we come from, and how we can live optimally.

The trajectory of DTC genetic testing over the last dozen years offers science and technology studies (STS) scholars a rich site at which to examine institutionalization – the process by which objects or practices circulate in regulatory and other types of organizations and through this process come to be understood as normative or “regular” facets of the social world. The DTC genetic testing case is informative as well because it takes place in the context of today’s robust neoliberalism and thus sheds light on the effects of the twinned-forces of deregulation of various institutional domains concurrent with the diminution of social welfare programs for healthcare and other services (Moore, Kleinman, Hess and Frickel 2011).

Additionally, the DTC genetic testing case provides a productive contrast with one of the more well-studied trajectories of institutionalization: the pharmaceutical market. With pharma, a significant aspect of the institutionalization process precedes the introduction of a product into the marketplace. When a drug enters the market, the product reflects the outcome of months or years of institutionalization, including in the form of laboratory science, clinical trials, the scrutiny of regulatory agencies (e.g., the United States Food and Drug Administration or FDA), and the framing of an illness and its treatment on the part of varied stakeholders (for example, social movements, patient advocates, and professional associations) (Epstein 1996, Dumit 2012).

Both over-the-counter and prescription pharmaceuticals have been directly advertised to consumers for decades and, in some ways, this practice both anticipated and precipitated the rise of DTC genetics. The origins of DTC DNA services lie at the juncture of two sociotechnical processes – molecular biology and supercomputing; these institutional predecessors of
today’s commercial genetic testing are analogous to some initial aspects of pharmaceutical development. Yet there are important differences in the institutionalization processes of these products that are worth noting: In contrast to pharma, the DTC genetic services industry was introduced by a set of actors – including businesspersons, investors, and scientists – whose scientific claims and products went mostly uninterrogated by outside reviewers or other types of checks and balances and received scant governmental regulation and ethical oversight. Consequently, efforts to institutionalize DTC DNA testing have mostly come after products and services have entered the marketplace. And, in contrast with pharma, customers and industry leaders have been able to play sizeable – if uneven – roles in this process.

Whether institutionalization occurs before or after the introduction of a commercial product, it enables classification – the sorting of new or contested objects and entities into classes, categorical boundaries, or architectures of social meaning. Because the introduction of commercial DNA testing proceeded with little external oversight, the classification of this new commercial entity – by state and federal agencies, consumers, industry professionals, and others – remains in formation. Boundaries are actively under negotiation. With DTC genetic testing, institutionalization is evolving as the tests do, making the dynamics of this process readily observable by scholars.

In the face of this regulatory lag, purveyors and consumers of DTC genetic testing may seek to shape the course of institutionalization. When enterprises and organizations are established with a low regulatory threshold, it may be the industry insiders themselves who initiate the institutionalization process. Anticipating regulation, they may seize the opportunity to set the terms of their own surveillance, as did some entrepreneurs who pioneered some of the first commercial genetic ancestry testing services in the United States (e.g., Kittles and Shriver 2004, also see Wagner 2012). On the other hand, genetic testing companies may capitalize on the lack of clarity about the classification of their products to resist institutionalization and create their own boundaries and norms: Some purveyors of DTC genetics have claimed that tests should be understood as personal, leisure pursuits that are non-medical or recreational and, therefore should not fall under the stringent regulatory schemes of agencies like the FDA (e.g., Lee 2013). Similarly, as we describe, consumers may want to keep regulatory institutionalization at bay for fear that it will restrict their access to genetic data, as was the case when federal agencies held hearings on DTC DNA testing several years ago. Consumers testified powerfully about their “right” to their own genetic information, free from government oversight (see our discussion below and also FDA 2010, Vorhaus 2010, Lee 2013).

DTC genetic testing’s categorical dynamism presents STS researchers with a challenge. How can scholars study a social phenomenon that is in formation, that may defy classification, or that vacillates between numerous institutions and organizations? One tried-and-true strategy for dealing with this challenge is to fix an object and study it within a single institutional location. For example, medical sociologists are most likely to study diagnostic genetic technologies and may do so at a physician’s office or among one group of patients (Atkinson, Parsons and Featherstone 2001). But genetic data is never simply one kind of information. Even if the outcome of genetic testing is supposed to be solely for medical use, the inherent nature of DNA means that it also always contains information about one’s health and may also be deemed to be informative for ancestry inference or in a criminal justice setting, even if these uses are not intended. The growing, problematic use of “familial searching” in criminal investigations, such as that leading to the apprehension of the BTK and Grim Reaper serial murderers – that brings the relatives of crime suspects who are disproportionately members of poor communities of color, under unwarranted police surveillance – is a case in point.

A flexible analytical approach is needed to account for the inherent characteristics of DNA
that make it informative in numerous contexts and for the emergent, liminal nature of forms of DTC genetic testing. Much like the shift from sociology in medicine (e.g., sociologists serving an uncritical supporting role to physicians and medical education) to the sociology of medicine (a perspective that brings sociological approaches to bear on medical professions, claims, expertise, authority, etc.) (Chaska 1977), STS scholars should not take all of our analytic cues from the genetic testing industry and the categorical claims it makes about its DTC services.

“The social life of DNA” (Nelson 2010, Wailoo, Nelson and Lee 2012) perspective is a more apt way of describing and analyzing the relatively recent phenomenon of DTC genetics. In keeping with anthropologist Arjun Appadurai’s methodological mandate that it is by attending to “the social life of things” – “things in motion” – that we can bring “human and social contexts” into view (Appadurai 1986), in this chapter, we track one DTC genetic test product in order to understand how meaning and norms accrue to it through this flow. Here we also follow Sarah Franklin and Celia Roberts’ elaboration of “the social life of PGD” (preimplantation genetic diagnosis) in their book Born and Made: An Ethnography of Preimplantation Genetic Diagnosis. Here the social life approach involves “researchers immers[ing] themselves in a range of different contexts to collect data about a particular object of inquiry, ‘following it around’ to build up a kind of hyperstack of definitions, images, representations, testimonies, description, and conversations…” (Franklin and Roberts 2006: xix). Franklin and Roberts offer a model of “how to account for the social dimensions of new biomedical technologies” (2006: xv) by thickly describing and analyzing these entities and their social circulation.

Our understanding of the institutionalization of an emergent technology and social practice such as DTC genetic testing can be enhanced by the “social life” approach. Because DTC genetic testing is both emergent and transverses categories and boundaries, the descriptive and analytic moves proposed by Appadurai, Franklin and Roberts are apt. Moreover, for genetic testing in particular, a social life of DNA perspective can also help to highlight the symbolic qualities with which we imbue genes and which partly derive from its use as a social explanation in many fora simultaneously (Nelkin and Lindee, 1995).

And, most importantly, this perspective attends to the particular physical properties of DNA that help to constitute how we make meaning of and with it. For, genes are omnipresent; they contain multitudes. A social life of DNA perspective offers a way to conceive how the techniques and logics of genetics (especially, the centrality of ideas of kinship; bio-banks and the database; statistics and probability; and molecular scale) are engaged in myriad social projects that may both abide and confound institutionalization. A second property of genes is that they are transitional. Genetic tests and the data they yield move between institutions and organizations, being engaged in various uses ranging from “optimization” to health to “security.”

A social life of DNA perspective also helps to account for the boundary blurring that attends the low institutionalization of DTC genetic tests and, by following the circulation of them at varied sites, helps to bring into relief how institutional boundaries take shape, recombine, and collapse. Additionally, following these tests and the contexts in which they draw meaning is precisely what allows us to see how DTC genetic testing does not abide the domains and boundaries that both entrepreneurs and social scientists – for very different reasons – endeavor to put around them.

Focusing on the well-known genetic testing company 23andMe, this chapter charts one course of the institutionalization of DTC genetics. We first briefly describe the technical facets of the spectrum of DTC genetic tests and the socio-cultural meanings that they engender. Next, we describe the boundary crises produced around so-called “recreational” genetic tests that are not merely an idle pursuit and that, furthermore, do not abide the categorical distinctions. In the second half of the chapter, we explain the current framework for regulation of DTC genetic
testing in the U.S., returning to the specific case of 23andMe and describing struggles over the regulation of this (and similar) company’s services. In closing we discuss what the regulatory struggles over 23andMe suggest about the institutionalization of new technologies.

**Direct-to-consumer genetic testing**

The human genome is a composite. A central conceit of the Human Genome Project was that we could derive a great deal of information – indeed, life’s ultimate data – by deciphering the genetic signatures of a select, unidentified and multicultural group of five persons: three women and two men. (This group was rumored to have included Craig Venter, the scientist who was a driving force behind the completion of this ambitious research endeavor). On the summer day in 2000 when the successful drafting of the human genome was announced, President Bill Clinton proclaimed that this multicultural, multiracial sample of DNA signatures highlighted “our common humanity” (White House 2000). The Human Genome Project confirmed that humans are 99.9% alike. But in the arenas of biomedical and scientific research, it was our supposedly uncommon genetic traits that were said to matter most of all, because even a 0.1% difference is meaningful in the context of the more than three billion base pairs that are the building blocks of human DNA. Concomitant with this development in genetic science was growing concern in the 1990s about disparities in health outcomes and research inclusion by race and gender and, soon after, rising support for research into the causes of these inequalities. To some minds, genetics research was poised to offer a biological explanation for the persistence of this form of inequality.

**DTC Genetics: not just fun and games**

The emergence of direct-to-consumer genetic testing in recent years has been considered of limited use to researchers across the disciplines. Natural and social scientists note that DTC genetic testing is not real science compared to survey-based genetic testing. This position has some merit, as these tests do not meet clinical research validity standards, and the company databases to which DTC genetics companies compare customer DNA are proprietary and therefore not subject to verification or refutation from other researchers or genetic testing companies who use different statistical assumptions, algorithms, or reference databases. Bioethicist and legal scholar Hank Greely, for example, contends that DTC DNA testing companies too often “invoke science’s power while skip[ping] the caveats” and “without accepting its limits.”1 The purveyors of these commercial tests support this position as well, but for entirely different reasons: they market testing as recreational or personal – and not as medical testing or clinical research – in part to avoid regulation of their practices. As a result, DTC genetics testing occupies a complex social space: it uses the language of science for marketing, yet the testing systems do not generate data that other scientists can verify.

It is perhaps unsurprising then that some of the earliest work in the social studies of genetics has explored its medical implications. STS scholars have focused intently on medical genetics, including some of the most influential work in the social sciences of genetics. For example, Abby Lippman coined the term “geneticization” and defined it as “an ongoing process by which differences between individuals are reduced to their DNA codes, with most disorders, behaviors and physiological variations defined, at least in part, as genetic in origin” (Lippman 1991).2 Notably, she elaborated this concept through feminist, sociological analyses of new reproductive technologies. Sociologist Troy Duster’s (1990) classic book, *Backdoor to Eugenics*, forewarned of the detrimental implications of a turn to DNA as an explanatory
catchall, and of the consequences of an emergent public health genetic screening apparatus. The work of Lippman, Duster and others is obviously concerned with the big questions about the social implications of geneticization, and these works set a critically important research agenda. Yet, these ideas emerged from scholars’ engagement with a medical genetics perspective that failed to anticipate the wider uses of genetic analysis, especially the ways in which they would operate without the expertise of medical professionals and without regulatory oversight.

The medical focus of STS scholars of genetics has meant that our tools for analyzing genetic ancestry testing and other forms of commercial genetic testing are underdeveloped. Writing in *Genetics in Medicine*, Jennifer Wagner and collaborators underscore this point, noting that “[e]xpert discussions and formal reviews of the DTC genetic testing industry have generally omitted an entire sector of the industry: companies that offer DNA ancestry tests” (2012: 586). Although DTC tests may be a leisure pursuit to some, they are not simply fun and games. The introduction of direct-to-consumer genetic testing over the past 15 years has spurred an evolution (if not, a revolution) in how we think about our selves and our communities. Like DTC pharmaceutical advertising introduced in the U.S. in the 1990s, some genetic testing can be requested by a health consumer but must be provided by a physician, such as Myriad Genetics’ BRACAnalysis test which was first introduced in 1993. Yet DTC genetic testing has produced new relationships within consumers and between consumers and experts. Here we focus on DTC tests that do not require mediation by a third expert party in either the testing process or in the disclosure of results.

The DTC genetic testing field

DTC genetic testing companies give their services colorful brand names such as Ancestry Painting and AncestrybyDNA. For the purposes of this essay, these tests may be sorted into two broad, overlapping clusters: health or “optimization” of one’s biology (Rose 2007: 6), and genealogy, ancestry and identity. In the U.S., commercial DTC genetics ventures began to emerge in 2000 with the founding of the genealogical testing company Family Tree DNA. In 2003, one study reported that there were seven DTC testing companies that broadly provided health information and close to sixty that offered some form of “identity” testing. By 2008, another report documented that “more than two dozen websites (including three of the original seven) offer more than 50 health-related tests to consumers” (Hogarth, Javitt and Melzer 2008: 165). There has been comparable growth in DTC genetic ancestry testing companies. In 2004, there were eleven companies offering this service; three more companies had entered the field by 2008. By 2010 “there were 38 companies selling a wide variety of DNA ancestry products, packages, and services.” In addition to Family Tree DNA, other early players in the genetic ancestry testing field include (or included) African Ancestry, deCODEme (deCode Genetics), the Genographic Project (a Family Tree DNA partner) and Gene Tree (which is no longer in operation). 23andMe is now one of the leaders in health-related testing, but like deCode it provides genealogical and health analysis under the same umbrella.

Rather than taking up the DTC genetic testing companies’ technical or brand descriptions, for STS scholars the tests are perhaps better classified according to the type of information each imparts and thus, the social meaning or action it enables on the part of the consumer. Nelson’s multisited ethnographic fieldwork in the U.S., that took place between 2003 and 2009 with African Americans consumers of DTC genetic testing, revealed that consumers purchase specific genetic tests in order to fulfill specific “genealogical aspirations” that may include affirmation of a multiethnic ancestry or evidence of “membership” in a certain racial or ethnic community (Nelson 2008a, Nelson 2008b). With these desires in mind, companies that sell...
DNA analysis for genealogical purposes can be said to offer three principal tests: ethnic lineage, racio-ethnic composite, and spatio-temporal. These three titles are a better fit than the brand names for what the tests actually offer by way of information to consumers. And consumers purchase the tests that best fit with the information they seek. All DTC ancestry tests do not provide the same information. Some allow affiliation with a particular nation-state, for example, while others offer inferred membership in a racial group or ethnic community.

Ethnic lineage testing draws on the distinctive features of Y-chromosome DNA (Y-DNA) and mitochondrial DNA (mtDNA) to infer consumers' ancestral links to contemporary nation-states or ethnic groups. Y-DNA is transmitted virtually unchanged from fathers to sons and can be used to trace a direct line of male ancestors. mtDNA, which is understood to be the energy catalyst of cells, is passed to both male and female children exclusively from mothers and is useful for tracking matrilineage. With both types of ethnic lineage testing, a consumer's DNA is searched against a testing company's reference database of genetic samples. If the sample and the reference DNA match an established number of genetic markers (typically eight or more), an individual can be said to have shared a distant maternal or paternal ancestor with the person who was the source of the matching sample in the reference group. Most DTC genetic testing companies offer ethnic lineage testing, including African Ancestry, Family Tree DNA, and 23andMe. A typical ethnic lineage result may inform a test-taker that her mtDNA traced to the Mende people of contemporary southern Sierra Leone or, more generally, to a region in Western Europe.

With spatio-temporal testing, a consumer's DNA sample is classified into a haplogroup (sets of single nucleotide polymorphisms [SNPs] or gene sequence variants that are inherited together) from which ancestral and geographical origins at some point in the distant past can be inferred. This form of analysis was made possible by the ambitious Y-DNA and mtDNA mapping research that resulted in theories about the times and places at which various human populations arose (Cann et al. 1987, Cavalli-Sforza et al. 1994). Several DTC companies offer this haplogroup information, including National Geographic’s Genographic Project. Based on a match with the mtDNA-derived H haplogroup, for example, a customer employing this test can receive a result indicating that her ancestors lived in Southwest Asia or the Middle East 20,000 years ago or more. Because these tests provide very broad results that apply to large portions of human communities, consumers using them are less interested in being matched to a specific ethnic group or nation-state than to their regional origins or their place in the larger history of human migration. This is one example of how technology and genealogical aspirations are co-constituted.

Racio-ethnic composite testing involves the study of nuclear DNA – which is unique to each person (identical twins excepted, although this is now being debated) and consists of the full complement of genetic information inherited from parents – for the purpose of making claims about one’s ancestry. A DNA sample is compared with panels of proprietary SNPs that are deemed to be ‘informative’ of ancestry. Algorithms and computational mathematics are used to analyze the samples and infer the individual’s admixture of three or four statistically constituted categories – sub-Saharan African, Native American, East Asian, and European – according to the presence and frequency of specific genetic markers said to be predominate among, but importantly, not distinctive of, each of the original populations. This form of analysis was developed and is principally offered by the AncestrybyDNA division of DNAPrint Genomics as well as by other companies that use its techniques, such as the Genetic Testing Laboratories in New Mexico and UK-based International Biosciences, and more recently, it has been offered by 23andMe. A hypothetical customer might learn that his or her composite is 80% European, 12% Native America and 8% East Asian, for instance. Each of these tests thus offers a different window into the past, and roots-seekers demonstrate different interests and preferences based on their genealogical aspirations.
Similar techniques can be used to elicit health-related information for an individual consumers’ DNA samples. This testing tends to analyze sets of SNPs that are deemed to provide information about propensity to some diseases. Although the tests are similar, regulatory controversy has mostly surrounded health-related testing. Critics have noted that these tests lack ethical and regulatory oversight and do not provide consumers with adequate information about the limitations of the tests. As Shobita Parthasarathy’s chapter describes, 23andMe has started to use its proprietary customer information for research studies, a development that raises concerns about informed consent and bioethical oversight.

**Regulation of DTC genetic tests**

**The current framework**

DTC genetic testing remains a largely unregulated field, either by federal or state authorities. What consumers are purchasing can vary widely from company to company, and the information that they are obtaining can range from a precise analysis of a SNP linked by extensive research with the development of a disease, to data about a number of other characteristics unrelated to health or illness that are, at best, not well-supported by research and generally falls under the umbrella of “recreational genomics.”

Legal and regulatory experts have been calling for the development of a federal regulatory schema for DTC genetic tests, and genetic tests generally, for nearly a decade, but despite the widespread concern, little action has been taken to address this growing field until quite recently (e.g., Javitt, Stanley and Hudson 2004, Solberg 2008, Conley, Doerr and Vorhaus 2010, Schlanger 2012).

In the absence of a federal regulatory framework, states have written their own laws, and these vary widely. The state legal landscape looks like a patchwork of mismatched pieces. For instance, some states only permit physicians and medical professionals to order DTC tests, and this effectively prohibits this testing by negating any benefits to consumers by directly ordering them. Some states, on the other hand, are actively regulating DTC testing, while other states remain silent on the issue (effectively permitting them) (Novy 2010, Drabiak-Syed 2010). Further, how each state defines the tests – “medical,” “clinical,” or “laboratory,” for instance – impacts who is permitted to order DTC tests and how. This legal patchwork leaves both consumers and companies wary about what laws apply to them and how. If a multi-state family, for instance, wanted each person to order a DTC genetic test, it may not be technically permissible for each of them to do so from their home states. The enforcement of these varied laws is questionable, which leaves consumers with little to rely on for assurance about the quality of the tests and possible social ramifications at the family level.

The federal government has the authority to regulate DTC genetic tests through various agencies, but has not yet done so systematically. Currently, there are at least three possible avenues for regulation that are not being fully utilized. First, the Clinical Laboratories Improvement Act of 1988 (CLIA) requires the federal government to certify laboratories that perform testing regarding the diagnosis, prevention, or treatment of any disease; however, the scope of CLIA and its requirements do not match the needs of DTC genetic tests. Next, the Federal Trade Commission (FTC) has the ability to regulate false and misleading claims, but it has not taken action to regulate the field of DTC genetic testing. Finally, the Food and Drug Administration (FDA) has the authority to regulate medical devices and laboratory developed tests (see, e.g., Javitt 2007). Though the FDA has done little to date to regulate the vast majority of DTC genetic tests, the agency has recently taken steps in this direction, which will be discussed below.
One possible, but unlikely avenue of further regulation is additional governance of the laboratories. All laboratories performing “clinical genetic testing” must be certified under the Clinical Laboratories Improvement Act of 1988 (CLIA), which is implemented by the Centers for Medicare and Medicaid Services (CMS). CLIA imposes “quality standards for all laboratory testing to ensure the accuracy, reliability and timeliness of patient test results regardless of where the test was performed” (42 U.S.C. § 263a). Unfortunately, however, “accuracy” and “reliability” as they have been applied to other laboratory tests are not defined in such a way as to be useful for genetic tests. In particular, CLIA only assures analytic validity and “does not address clinical validity or claims made by the laboratory regarding the tests.” In other words, though a lab may decode a particular gene sequence accurately, CLIA does not certify that the string of As, Cs, Ts, and Gs are actually linked to the disease or trait that the company claims that they are, let alone whether this information is usable by a patient or a health professional. Ensuring the analytic validity, the clinical validity, and the utility of these tests is of central concern to those calling for regulation (Solberg 2008).

As we noted, the FTC has the capacity to prohibit false and misleading claims made by DTC genetic testing companies. Though the FTC has the jurisdiction to administer consumer protection laws, and it exercises that jurisdiction in a variety of arenas, it has neglected to take meaningful action against claims of clinical validity made by DTC genetics companies. Despite consumer complaints, the only action taken by the FTC to date is issuing a warning in 2006 to consumers to be skeptical of claims made by genetics testing companies and to speak with a physician before and after taking such a test (Drabiak-Syed 2010, Novy 2010).

The most likely avenue for regulation of DTC genetic tests is by the Food and Drug Administration (FDA). Understanding several regulatory schemas of the FDA is critical to understanding why DTC genetics tests have heretofore not been regulated, and how they are likely to be regulated in the future. Due to questions surrounding genetic information itself – what does it measure and how? is it risky? can it harm you? – as well as loopholes in the regulation, shown below, genetics companies have not yet been governed by the same provisions required of other laboratory tests transmitting biological information.

The Medical Device Amendments of 1976 gave the FDA broad authority to regulate the safety and effectiveness of medical devices, which it defines as any “instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent or other similar or related article, including any component, part or accessory” that is “intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease” (The Medical Device Amendments, 21 U.S.C. § 301 et seq.). How much regulation is imposed upon a manufacturer of a device depends on how risky a device is deemed. Medical devices are grouped into three categories of risk, Class I devices, which have the least oversight, Class II devices, which have moderate oversight, and Class III devices, which have the most oversight (The Medical Device Amendments). Class I devices are subject only to “general controls,” which include good manufacturing practices, record keeping, and filing specified reports with the agency. Class II devices are subject to “special controls,” such as performance standards, ongoing surveillance, and specific guidance and interventions by the agency. Class III devices are subject to pre-market approval (PMA), which means that the agency must approve the device before it is distributed to the public.

Devices that entered the market after 1976 were presumptively Class III, and thus required PMAs, unless they could show that they were “substantially equivalent” to a device that came on the market before 1976 – a “predicate device.” To circumvent the lengthy and expensive PMAs and show “substantial equivalence,” a manufacturer would submit what is known as a “510(k).” As it became more and more difficult for manufacturers to show substantial equiva-
lence with pre-1976 predicate devices, it became clear that new, less-risky devices should be able to apply for 510(k) without a predicate device. In 1997, Congress amended the law to permit “de novo” 510(k) classification for low- and moderate-risk devices (The FDA Modernization Act of 1997, 21 U.S.C. § 513 (f)(2)). As we will show below, this amendment became critical for DTC genetic tests nearly 15 years later.

Any in vitro diagnostic (IVD) can be regulated as a medical device. An IVD is defined as:

The reagents, instruments and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat or prevent disease or its sequelae. Such products are intended for use in the collection, preparation and examination of specimens taken from the human body.

21 C.F.R. § 809.3(a), In Vitro Diagnostic Products

The FDA regulates IVDs in three categories: general purpose reagents, analyte specific reagents (ASRs), and test kits. General purpose reagents are more typical chemical reagents that are available in a laboratory, and they are categorized as Class I devices. ASRs are more complex reagents, such as antibodies, specific receptor proteins, and nucleic acid sequences, which function through a specific binding mechanism to a biological sample. Though most ASRs are Class I, some ASRs are Class II and III. Regardless of classification, however, the FDA restricts ASRs sale, distribution, and use, to specifically permitted manufacturers and laboratories. A third IVD regulated by the FDA are “test kits,” which can include bundled reagents, a microassay, or another testing platform (Javitt 2007).

From these regulations, it might appear logical that the FDA could regulate DTC genetic tests as test kits, but historically, the FDA has not regulated what are considered laboratory developed tests (LDTs), beyond regulating their ASRs. LDTs are those test kits that are created and used completely in-house, and as such are sometimes called “home brews” (Patsner 2008). The FDA has made statements that it, sometime in the future, may take steps to regulate LDTs more broadly, but it has not yet done so (Schlanger 2012).

Though many options may be available to the FDA to regulate DTC genetic tests, no widespread action has yet been taken. Proposed regulatory revisions to the current FDA schema include modifications to streamline DTC and CLIA oversight and to create an entirely new division in the FDA, separate from the medical device regulations, that would oversee and evaluate all “advanced personalized diagnostics” (Schlanger 2012: 404). In sum, though many experts have called for more regulation of DTC genetic tests and it appears that there is the legal authority to do so, little action has been taken at the state or federal levels to broadly regulate this growing field. This leaves consumers with, at best, an ambiguous patchwork of regulation covering a wide variety of products, and at worst, unscientific, misleading, or incorrect information about themselves and their families.

FDA and Congressional Action, 2006 to present

In 2006, the FDA sent out a series of “untitled” letters (a low-level warning) to several genetic testing companies requesting a variety of actions ranging from meetings and consultation with the FDA to submission of a de novo 510(k). The companies responded by altering their tests to make them completely in-house laboratory developed tests (LDTs), questioning the jurisdiction of the FDA, or ignoring its requests altogether.

In September 2006, in response to concern about genetic LDTs, the FDA issued draft guidance on its role regulating a subset of LDTs, in vitro diagnostic multivariate index assays.
These assays are characterized by their use of proprietary algorithms, often run through software, that generate patient-specific results based on multiple pieces of data derived from one or more in vitro assays (Javitt 2007). The FDA approved its first IVDMIA in February 2007, the Mammaprint test, which uses mRNA to determine the likelihood of breast cancer returning within five to ten years after an initial diagnosis. The company submitted data about a clinical trial, and the FDA approved Mammaprint with narrow intended use that reflected the limitations of that trial (Javitt 2007).

In 2006, the General Accountability Office (GAO), the investigative arm of Congress, made an unexpected intervention by doing a “sting” operation into four unidentified DTC genetic testing companies. GAO posed as fourteen individual consumers, although twelve of the DNA samples came from a nine-month-old female baby and two came from a forty-eight-year-old male. The results and recommendations of the companies investigated varied widely – in one case, the company recommended the same expensive “personalized” nutritional supplements for both the baby and the man (Piehl 2011). The sting revealed that there was little consistency between the testing companies. But even these alarming results of GAO’s sting operation did not result in the regulation of the DTC genetic testing industry.

Although critics of the unregulated growth of the industry continued to raise concerns from 2006 on, significant FDA and Congressional activity did not resume until 2010. In May of 2013, Pathway Genomics (Pathway) announced that it planned to sell mail-in saliva sampling kits directly to consumers at Walgreens stores nationwide (Schlanger 2012, Mullard 2012). The FDA responded by sending a letter to Pathway, warning it that its product was a medical device, and that it must comply with the standard regulatory obligations placed upon medical device manufacturers. Pathway defended its proposed action, but pharmacies refused to carry the test, temporarily resolving the FDA’s role. Pathway’s action also prompted the House Committee on Energy and Commerce (House Committee) to open an investigation into 23andMe, Navigenetics, and Pathway. Among the reasons for the investigation were to find out what exact tests companies were offering, how accurate the tests were, how consumers were being protected, and whether the companies were FDA compliant (Schlanger 2012).

The FDA sent letters to five more genetic testing companies in June 2010, 23andMe, Navigenetics, deCODE Genetics (deCODE), Knowme (pronounced “know me”), and Illumina, which were similar to the letter sent to Pathway. The letters stated that the companies’ tests were medical devices and thus subject to regulation by the FDA, but that the tests were not considered LDTs, because the tests were not made and used in-house. One month later, in July 2010, the FDA sent similar letters to fourteen additional genetics companies (totaling 20 altogether) (Schlanger 2012).

During the same summer, the FDA called a public meeting regarding the oversight of LDTs, during which it acknowledged its intent to regulate them but without stating how it would do so. At the public meeting in July, the FDA suggested it would take a “risk-based application of oversight” (Schlanger 2012: 394).

The same week as the FDA meeting, the House Committee held a hearing about the regulation of genetic tests and their effects on public health. At the hearing, GAO announced it had conducted a follow-up to its 2006 sting operation (Schlanger 2012, GAO Highlights 2010). This investigation involved four named companies – 23andMe, Navigenetics, Pathway, and deCODE Genetics. GAO used five people and submitted two samples for each person to each company (40 total tests). For each individual, one DNA sample was submitted with the individual’s age, race, and medical history, and one DNA sample was submitted with a fictitious age, race, and medical history. One participant’s DNA, for instance, was submitted both as a thirty-seven-year-old Caucasian woman with colon cancer and as a sixty-eight-year-old African American woman with breast cancer.
American woman with hypertension and diabetes. As with the 2006 study, the disease risk predictions received from the companies were “misleading and of little or no practical use” (GAO Highlights 2010). The disease risk predictions differed greatly both within the same company for the same DNA and disease and between the companies for the same DNA and disease. The companies justified the former by arguing that different algorithms are available to determine disease susceptibility for different racial and ethnic populations (23andMe 2010). This argument, however, contradicts other claims made by the companies, which purport to be able to determine racial and ethnic heritage as part of their genetics package. The results also differed greatly between companies. For instance, one donor, being tested for risk of leukemia, was found to have “below average,” “average,” and “above average” risk of developing the disease by the various companies (GAO Highlights 2010). Through its blog The Spitoon, 23andMe did not challenge any of the specific findings of the GAO report, but defended its results as sound – not only were the “As, Cs, Ts, and Gs” accurate and reliable, but disease risk predictions should be expected to vary from company to company – and called the GAO investigation “unscientific” (23andMe 2010).

Thus, while federal agencies tried repeatedly over the last several years to regulate the DTC genetics industry, confusion over the categorical boundaries of the tests – along with resistance on the part of both purveyors and consumers – held institutionalization at bay. Consumers were vocal during the FDA hearings, declaring their right to have access to genetic information about themselves and also their right to be free of state and federal constraint (FDA 2010, Vorhaus 2010). Industry leaders, for their part, countered claims that their tests were medical (thereby falling into a well-established regulatory apparatus) by resisting any label but the amorphous “non-medical” or “recreational.” Moreover, at least one company responded to the federal investigators claims that the tests were not scientifically valid, by calling into question the science of the government’s own researchers.

23andMe’s De Novo 510(k) Application

Several years later, after it had collected thousands of consumer samples and was poised to enter the market for medical and drug patents, 23andMe unfolded a new strategy. Once critics of the institutionalization of DTC genetics, this company became the state’s partner in this process. Following several years of behind-the-scenes conversations with the FDA, 23andMe applied in June 2012 for de novo 510(k) review of seven of its approximately 240 offered SNP-based genetic reports. The company stated that it intended to submit up to 100 more reports by the end of 2012 (The Burrill Report 2012, Mullard 2012). Such reports would be evaluated for both analytic and clinical validity, meaning that 23andMe can consistently and accurately identify gene sequences, and more challengingly, that it can validate its claims about correlations between specific genes and associated risks for developing diseases. These submissions were the first of their kind in the DTC genetics market. Moreover, according to Daniel Vorhaus of The Genomics Law Report, it could “represent the way forward for certain components of the DTC industry” (The Burrill Report 2012). Such a route to approval would have several advantages for 23andMe, primarily its ability to claim that they are the first, and for a time, the only FDA-approved DTC genetics company, and it would allow the company to set the terms of its own surveillance (and of competitors that will follow it). In the industry broadly, establishing that de novo 510(k) is a possible avenue for DTC genetic tests could encourage other companies that may have been wary of the more onerous pre-market approval process and it may make it a requirement for 23andMe’s competitors that may be less well-prepared to clear this stringent hurdle. In other words, it would set a course for institutionalization for the industry.
On November 22, 2013, however, the FDA issued a warning letter to 23andMe to immediately stop marketing its DTC genetic test or risk regulatory action such as seizure, injunction, and civil money penalties,” with which 23andMe stated it would comply (FDA 2013, 23andMe 2013). Under the regulatory framework, 23andMe failed to meet analytical and clinical validity requirements for de novo 510(k) approval, that is, it failed to validate the claims about correlations between specific genes and associated risks for developing diseases. This failure rendered the test a Class III device, which requires pre-market approval.

The warning letter details the lengths to which 23andMe went to receive a de novo 510(k) approval from the FDA — there were over fourteen meetings, hundreds of emails, and dozens of written communications (FDA 2013). The letter states that the FDA provided “ample detailed feedback” regarding analytical and clinical validity requirements (as well as suggesting modifications to the device’s label to meet requirements for certain uses), but that 23andMe failed to provide any of the studies necessary for de novo 510(k) approval (FDA 2013). Instead, 23andMe simultaneously ceased communications with the FDA and expanded the marketing claims and consumer base for its test. This extensive relationship between 23andMe and the FDA may reveal a belief, on the part of both organizations, that such tests could ultimately garner approval within the current regulatory framework. Indeed, this belief was common in the regulatory community (The Burrill Report 2012). Alternatively and perhaps cynically, this unusual alliance could belie 23andMe’s success in keeping regulatory boundaries blurred, allowing the company to proceed unregulated for as long as possible while it gained popular acceptance.

Can recreational genetic testing become institutionalized?

Several years of behind-the-scenes conversations and lobbying provided reason for those in the industry to believe that regulatory oversight could provide more benefits than costs. Overcoming the state-by-state patchwork of regulations, mollifying the uncertainty for some investors, and gaining the claims of “first” and “only” had the potential to outweigh the financial and ultimately regulatory costs of applying for de novo 510(k) approval. As one expert in the field stated, “Getting it through an FDA review process ... can have a validating effect for 23andMe in the eyes of thought leaders, opinion leaders, policy makers in the field that have been, many of whom have been, critical of the DTC model” (The Burrill Report 2012).

To pass muster under 510(k), the reports submitted by 23andMe would need to show both analytical and clinical validity. For prospective prediction of diseases, proving clinical validity could be possible – studies can be done to examine who, with that SNP, develops a particular disease. Moreover, the companies’ claims can be compared and contrasted with existing clinical research. But, for retrospective determination of racial and ethnic ancestry, it would be impossible to ever show a link between genes and the past, given that our ancient ancestors are not readily available for examination and the companies create proprietary algorithms that make idiosyncratic historical claims and categorical claims (e.g., the presence of a higher percentage of this SNP means one is Asian, with no accounting for how “Asian” is socially constituted) that cannot be validated without undermining the secrecy that contributes to brand identity and market share. It seems from this model that “clinical validity” as applied to prospective disease markers is irrelevant to retrospective ancestry testing.

This distinction between health-related disease prediction tests and recreational ancestry tests is highlighted by 23andMe’s response to the FDA letter. 23andMe stated that it will comply with the FDA by providing “raw genetic data without interpretation” for health-related tests, but that it would continue providing “ancestry-related information” (23andMe 2013).
Because the 510(k) process exists under the framework of medical device regulation, it is unclear if ancestry tests would ever be approved under the same process. Nevertheless, the legitimacy that would be afforded to 23andMe by an approval of its disease markers would likely have an effect, one way or the other, on the perceived legitimacy of its ancestry tests. On one hand, the imprimatur of the FDA on 23andMe's health-related tests could, in the minds of consumers, trickle down to the company's recreational genetic tests. It is also possible that some consumers would be turned off by ancestry tests that are unable to gain the validating stamp of the federal government. It seems unlikely, however, that all consumers would stop purchasing the ancestry tests, given their willingness to use the technology to date and eagerness to find "workaround[s]" to the FDA's 2013 action (Hensley 2013).

The DTC genetics testing companies have often claimed that their products are “informational” and “educational,” and not intended to provide a medical or health assessment (Popovsky 2010). It is likely that those products, such as ancestry testing, would continue to be defensively labeled “informational” by the companies.

Following its 510(k) submission, 23andMe wrote in their blog The Spitoon that they continue to believe that consumers “have a fundamental right to their personal genetic data” and that the data “will power a revolution in healthcare. But we also recognize that appropriate oversight of this industry can be a stepping stone on the path to realizing that revolution” (23andMe 2012). In the past, 23andMe has argued, “genetic information is a fundamental element of a person’s body, identity and individuality. As such, the rights that people enjoy with regard to financial, medical and other forms of personal information should apply to genetic information as well” (see Popovsky 2010: 76). In this way, the company articulates arguments from both the industry side and the consumer perspective to forestall institutionalization, even as it has sought a regulatory partnership with the FDA.

Conclusion

23andMe’s de novo 510(k) application for their DTC genetic tests highlights an era of rapid growth in the history of DTC genetic testing. By exploiting the boundary crisis between health and recreational genomics during a period of regulatory lag, the genetic testing company sought to negotiate the terms of its own surveillance and in the process attempted to define and expand the meanings and understandings of all of its products. By specifically applying for a 510(k) rather than PMA, 23andMe not only indicated that there is no substantially equivalent device — that it provides a sui generis service that has no regulatory analogue — but also that they believe that the product they offer is not risky and does not warrant stringent oversight. From a regulatory standpoint, an approval under these conditions would open the DTC genetic testing field quite a bit — by avoiding the higher categories of risk, many more applications would be sent to the FDA, with a regulatory imprimatur serving to vouchsafe the market. Further, being the first company in such a position, 23andMe would gain more credibility as being a pioneer in the field. As such, smaller companies having neither the FDA’s seal of approval nor the means to gain it may find it hard to survive in such a marketplace. Moreover, by gaining some federal regulatory stability that supersedes the state-by-state patchwork, 23andMe could attract more investors.

Through these various mechanisms of institutionalization, 23andMe sought to gain the legitimacy of the bureaucracy while they actually built it themselves. While consumers eager to gain insight into their health and ancestry, and believing it is their “right” to the tests, may, against the backdrop of a neoliberal assault on the welfare state, appear to be the primary beneficiaries of the growth of the DTC genetic test industry, the fact that 23andMe seeks to set the
terms of its own governance calls into question who or what is in the position of power. The tests that could to gain approval under the current regulatory framework are medical, but, as mentioned previously, such approvals are likely to have a “validating effect” on all products, that is, consumers would likely deem the entire company regulated, reliable, and trustworthy (The Burrill Report 2012). Thus, consumers are more likely to trust a company that has the FDA’s imprimatur on any of its products, including that company’s products for ancestry testing that are not currently regulated. Given what we know about why consumers purchase DTC genetic ancestry tests – in order to fulfill genealogical aspiration – and what we know about geneticization – how consumers can substitute DNA meanings for other explanations and understandings of society – the institutionalization of DTC genetic testing should proceed with, if not caution, at least a broad awareness of the biosocial implications.

Notes
6 Obviously, these categories are constructed by the DTC genetics companies in a fashion that seldom takes into account the fact that these categories are socially constructed or that the nations and borders to which they refer have changed repeatedly over human history. A thorough discussion of the limitations of genetic ancestry testing is provided by Nelson and collaborators; see Bolnick et al. 2007.
7 As this essay was going to press, the FDA ordered 23andMe to immediately stop marketing its DTC tests (FDA 2013). This development is discussed below.
8 23andMe’s Anne Wojcicki also testified against regulation on this day.

References
21 C.F.R. § 809.3(a). In Vitro Diagnostic Products For Human Use.


