



The Past, Present, and Future of Direct-to-Consumer Genetic Testing: What we have Learned and Why Increased Regulation is Warranted

Citation

Stephanie Bair, The Past, Present, and Future of Direct-to-Consumer Genetic Testing: What we have Learned and Why Increased Regulation is Warranted (March 2011)

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**The Past, Present, and Future of Direct-to-Consumer
Genetic Testing: What we have Learned and Why Increased
Regulation is Warranted**

**Submitted in satisfaction of the course requirement for
Food and Drug Law, January 2011**

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March, 2011**

Abstract

Almost a decade after the complete sequencing of the human genome, we have seen a proliferation of genetic testing services marketed directly to the consumer and purporting to use genetic information to generate individualized health information. These tests have been subject to only minimal regulation, despite the fact that scientists and policymakers have serious concerns about both the clinical effectiveness of the tests and the safety of releasing certain types of health information to the public without the supervision of a health care professional. Proponents of minimal regulation argue that the tests allow for patient autonomy and privacy of genetic information, while unburdened marketing of the tests encourages increased development and innovation of testing services. This article explores in depth both the benefits of direct to consumer genetic testing and the concerns arising from such tests, and concludes that particular safety and accuracy concerns warrant increased oversight of these tests. The article then goes on to evaluate the current regulatory framework under which direct to consumer genetic testing services operate, and finds that it is insufficient in light of these concerns. The article concludes that recent steps by the Food and Drug Administration (FDA) to exercise increased regulation over direct to consumer genetic tests are warranted and will provide the optimal amount of regulation for these tests.

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I. Introduction: the Human Genome Project and the advent of direct to consumer genetic testing

In 2003, the Human Genome Project released the completed sequence of the human genome.¹

The media and the scientific community at the time heralded this accomplishment as “the key to transforming medicine and understanding disease,”² predicting the usefulness of the human genome for the development of new treatments, the customization of drugs to individual genetic profiles, and the identification of individual propensities to develop specific diseases.³

Scientists also warned, however, that the sequencing of the human genome was simply the first step on a “long road”⁴ of scientific research and that “immediate major breakthroughs should not be expected.”⁵

The completion of the human genome opened a new era of human genetic and medical research. Riding this new wave of discovery have emerged a bevy of private companies offering what have come to be termed direct-to-consumer (DTC) genetic testing services.⁶ As the name implies, these tests are marketed directly to consumers and can be purchased and completed without the involvement of a medical health care professional.⁷ These tests are offered for a variety of purposes, from predicting a child’s eye color to determining an individual’s response to AIDS treatment.⁸ Most of these tests fall within a regulatory grey area; thus, the DTC genetic testing industry has to this point remained largely unregulated.⁹

¹ Wired.com, Human Genome Complete, <http://www.wired.com/medtech/health/news/2003/04/58471>.

² *Id.*

³ *Id.*

⁴ *Id.*

⁵ *Id.*

⁶ See, e.g., Justin P. Annes et al., *Risks of Presymptomatic Direct-to-Consumer Genetic Testing*, 363 NEW ENG. J. MED. 1100, 1100 (2010).

⁷ *Id.*

⁸ For example, the genetic testing service 23andMe provides information for both of these purposes with the purchase of a 23andMe genetic “health kit.” 23andMe.com, Health Reports: Complete List, <https://www.23andme.com/health/all/>.

⁹ See, e.g., Rebecca Andar Novick, *One Step at a Time: Ethical Barriers to Home Genetic Testing and Why the U.S. Health Care System is Not Ready*, 11 N.Y.U. J. INT’L L. & POL. 621, 624-631.

Almost a decade after the human genome has been sequenced, we are beginning to understand more about the risks and benefits of direct- to- consumer genetic testing. A detailed examination of these risks and benefits suggests that recent steps by the Food and Drug Administration (FDA) to comprehensively regulate DTC genetic tests as Class III medical devices requiring premarket approval¹⁰ are steps in the right direction, and will lead to increased safety, effectiveness, and public trust of the DTC genetic testing industry.

II. The science behind direct to consumer genetic tests

Direct to consumer genetic tests are marketed for a variety of purposes. Some tests are specifically marketed as a means of ascertaining genetic ancestry or other relationship-based information, such as the gender of an unborn child.¹¹ Also popular, and the focus of this paper, are the health-based tests, which provide a range of health and medical information. Specifically, pharmacogenetic tests purport to provide information about the suitability and efficacy of a particular drug for the individual consumer.¹² Predictive genetic tests are marketed as a means of obtaining individualized risk assessments for the acquisition of a particular disease or set of diseases,¹³ and nutrigenetic tests provide individualized nutrition and lifestyle information based on a consumer's genetic profile.¹⁴ Many testing companies offer all three of these services.¹⁵

The science of genetic testing is based on the simple idea that an individual's personal

¹⁰ In September 2010, FDA sent letters to five DTC genetic testing companies, requesting that these companies submit premarket approval applications for their products. See FDA.gov, Medical Devices Letters to Industry, <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/ucm111104.htm>.

¹¹ For example, the company Ancestry.com offers a genetic test to “help you find genetic cousins and expand your family tree.” Ancestry.com, DNA Testing by Ancestry.com, <http://dna.ancestry.com/welcome.aspx>.

¹² See, e.g., Novick, *supra* note 8, at 632-3.

¹³ *Id.* at 633-4.

¹⁴ *Id.* at 632.

¹⁵ For example, the genetic testing service Navigenics will “analyze[] your DNA for genetic risk markers associated with a wide variety of health conditions and medication responses,” so that a consumer can “personalize [his] health strategies.” Navigenics.com, Conditions and Medication Responses, http://www.navigenics.com/visitor/what_we_offer/conditions_we_cover/.

genetic makeup can provide a wealth of varied and valuable information. Although this is certainly true, an understanding of the specific scientific underpinnings of these tests is necessary to understand both their strengths and their limitations.

A. The genetics of genetic testing

The “human genome” refers to the genetic information encoded by the 23 pairs of chromosomes found in the nuclei of most cells in the human body.¹⁶ Chromosomes are composed of two intertwining strands of deoxyribonucleic acid (DNA), and each strand of DNA, in turn, is composed of a series of nucleotides.¹⁷ A nucleotide (adenine, thymine, cytosine, or guanine) in a single strand of DNA is bonded to a complementary nucleotide on the second intertwined strand, forming a base pair.¹⁸

Mutations in genetic information can occur in a variety of ways.¹⁹ Mutations may occur during cell division as a copy of an organism’s genetic information is made and included in the new cell.²⁰ Genetic information may be added or deleted from a gene, or base pairs may be rearranged within a gene.²¹ During this copying process, single nucleotides may also be miscoded (for example, an adenine may be replaced by a cytosine), leading to what are known as single nucleotide polymorphisms (SNPs).²² SNPs are inherited from parent to child, and continuing research is divining correlations between the identity of specific SNPs and various health-related measures, such as susceptibility to certain diseases or responsiveness to certain drugs.²³

¹⁶ ELDRA PEARL SOLOMON ET AL., BIOLOGY G-16 (4th ed. 1996).

¹⁷ *Id.* at 272-7.

¹⁸ *Id.*

¹⁹ *Id.* at 303-9.

²⁰ *Id.*

²¹ *Id.*

²² JOHN M. BUTLER, FORENSIC DNA TYPING: BIOLOGY, TECHNOLOGY, AND GENETICS OF STR MARKERS 182 (2d ed. 2005).

²³ *Id.*

Companies currently offering DTC health-based genetic tests rely on SNPs to provide inexpensive genetic testing. Rather than sequencing an individual's entire genome, which is still infeasible due to cost, DTC genetic testing companies use a "SNP chip" to target particular SNPs in an individual's genetic material.²⁴ By determining the identity of a range of an individual's SNPs, these companies, drawing on current scientific research associating particular SNP profiles with health-related measures such as susceptibility to disease, purport to provide individualized health information to the consumer.²⁵ Each type of genetic test uses a SNP chip to obtain genetic information and then draws on research from the relevant fields to draw potentially useful conclusions.

B. Pharmacogenetic tests

Pharmacogenetic tests use current research associating particular genetic profiles with responsiveness to specific drugs to provide individualized drug responsiveness information to the consumer.²⁶ For example, certain SNPs in the CYP2C9 gene have been found to be associated with an individual's ability to metabolize Warfarin, a drug prescribed as a blood thinner.²⁷ This association has been well-documented, and in fact the FDA has stated that genetic testing could play an important role in determining individualized dosages of Warfarin.²⁸ The DTC genetic-testing company 23andMe provides information to consumers about predicted Warfarin responsiveness based on the consumer's variant of the CYP2C9 gene.²⁹ The company also

²⁴ R. RAPLEY R. & S. HARBRON, *MOLECULAR ANALYSIS AND GENOME DISCOVERY* (2004).

²⁵ 23andMe, for example, states that their DNA chip "genotypes hundreds of thousands of SNPs at one time," and the company also "hand-pick[s] tens of thousands of additional SNPs of particular interest from the scientific literature and adds their corresponding probes to the DNA chip... to provide personal genetic information." 23andMe.com, How Does 23andMe Genotype my DNA?, <https://www.23andme.com/you/faqwin/chip/>.

²⁶ See, e.g., Novick, *supra* note 8, at 632-3.

²⁷ See, e.g., Wadelius et al., Association of Warfarin Dose with Genes Involved in its Action and Metabolism, 121 *Hum. Genet.* 23, 23-34 (2004).

²⁸ FDA.gov, Critical Path Initiative- Warfarin Dosing, <http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/FacesBehindCriticalPath/ucm077473.htm>.

²⁹ 23andMe.com, Warfarin Sensitivity-Sample Report, <https://www.23andme.com/health/Warfarin-Coumadin->

provides predictive response information for 18 other treatments and drugs, ranging from information regarding an individual's susceptibility to heroin addiction, to information about an individual's predicted response to Hepatitis C treatment.³⁰ Although some of the associations upon which this information is based-- including the association between Warfarin metabolism and CYP2C9 variants-- are well-grounded in many years of research, other associations are much more tentative and are based only upon a single recent study.³¹

C. Predictive tests

Predictive tests, as their name implies, are marketed for the purpose of "predicting" whether an individual will develop a specific disease in his lifetime based on his genetic profile.³² When evaluating genetic susceptibility for disease, an important distinction must be made between the Mendelian, or monogenic, diseases on the one hand and the complex, or polygenic, diseases on the other.³³ Monogenic diseases are hereditary diseases that are caused by a mutation in a single gene.³⁴ These diseases may exhibit complete penetrance, meaning that all individuals carrying the relevant mutation will exhibit symptoms of the disease at some point in their lives.³⁵ Familiar examples of monogenic diseases include Huntington's disease and cystic fibrosis.³⁶ In contrast, complex or polygenic diseases do not exhibit Mendelian inheritance patterns and are thought to arise due to a complex interaction of several genetic and environmental influences.³⁷ Associations linking particular genetic mutations to polygenic disease susceptibility are

Sensitivity/.

³⁰ 23andMe.com, Health Reports: Complete List, <https://www.23andme.com/health/all/>.

³¹ For example, 23andMe's association between genetics and response to a subset of antidepressant drugs is based on a single study. 23andMe.com, Antidepressant Response- Sample Report, <https://www.23andme.com/health/Antidepressant-Response/>.

³² See, e.g., Novick, *supra* note 8, at 633-4.

³³ MICHAEL WINK, AN INTRODUCTION TO MOLECULAR BIOTECHNOLOGY 456 (2006).

³⁴ *Id.*

³⁵ MUIN J. KHOURY ET AL., HUMAN GENOME EPIDEMIOLOGY 38 (2d ed. 2010).

³⁶ *Id.*

³⁷ WINK, *supra* note 32.

necessarily probabilistic; because the development of the disease depends on the interaction of a number of known and unknown factors, the most that can be done is to estimate increased risk of the disease. This estimate is derived from population studies comparing individuals carrying a specific variant of a gene of interest with others who do not carry that specific variant.³⁸ Common examples of polygenic diseases include heart disease and Type II diabetes.³⁹

Many DTC predictive tests available on the market today evaluate an individual's susceptibility to polygenic rather than monogenic diseases. Thus, these tests can only provide estimations of risk based on population data.⁴⁰ This is again accomplished by linking SNP profiles in the individual consumer with associations between particular SNPs and susceptibility to certain diseases. The genetic testing service 23andMe offers predictive information for 95 diseases and conditions, including "back pain," attention deficit hyperactivity disorder, schizophrenia, lung cancer, and heart disease.⁴¹

D. Nutrigenetic tests

Nutrigenetic tests are similar to predictive tests in that they analyze an individual's risk of disease based on his genetic profile. The testing company then goes one step further by providing individualized diet and lifestyle recommendations based on this analysis, with the goal of reducing the individual's risk.⁴² For example, if the genetic test results determined an individual to be at increased risk for developing heart disease, the test results would return diet and lifestyle recommendations based on the current scientific understanding of reducing risk for this disease. Thus, the consumer would be advised to exercise, avoid tobacco, and eat a diet low

³⁸ D.J. Galton & G.A.A. Ferns, *Genetic Markers to Predict Polygenic Disease: a New Problem for Social Genetics*, 92 QUART. J. MED. 223 (1999).

³⁹ *Id.*

⁴⁰ Galton & Ferns, *supra* note 37.

⁴¹ 23andMe.com, Health Reports: Complete List, <https://www.23andme.com/health/all/>.

⁴² See, e.g., Novick, *supra* note 8, at 632.

in saturated fat and full of fruits and vegetables.

III. Benefits and drawbacks of DTC genetic testing: implications for regulation

For many years, scientists and policymakers have discussed the potential benefits and drawbacks of DTC genetic testing.⁴³ The concerns of those who argue for increased regulation of DTC genetic tests, foremost among these concerns about accuracy and clinical effectiveness of the tests and patient use of results, provide a strong rationale for increased regulation.⁴⁴ Those who believe that DTC genetic tests should continue to be offered with minimal regulatory intervention often point to the benefits of patient autonomy, privacy, and ex ante effects on test development;⁴⁵ however, a closer inspection of these potential benefits reveals that they may not actually be achieved through the unregulated marketing and use of DTC genetic tests, and may in fact be stimulated (or at least not undermined) by increased regulation.

A. Concerns with DTC genetic tests

1. Consent

A threshold concern with DTC genetic tests involves the concept of informed consent.⁴⁶ The idea of obtaining informed consent from a patient before proceeding with a medical procedure or treatment is one that is well-established in health jurisprudence.⁴⁷ A doctor must discuss the risks and benefits of a proposed procedure with a patient and allow the patient to ask questions.⁴⁸ A doctor must also disclose possible alternative procedures and the risks and benefits of such alternatives.⁴⁹ The rationale behind such a requirement is the protection of an individual's freedom to choose those procedures which she will undergo after having considered the relevant

⁴³ See, e.g., A.L. Maguire et al., *Personal Genome Testing*, 330 SCIENCE 181-2 (2010).

⁴⁴ *Id.*

⁴⁵ *Id.*

⁴⁶ See, e.g., Novick, *supra* note 8, at 635-40.

⁴⁷ See, e.g., L.B. Andrews, *The Rationale Behind the Informed Consent Doctrine*, 1 J. MED. PRAC. MGMT. 59-65 (1985).

⁴⁸ Novick, *supra* note 8, at 635.

⁴⁹ *Id.*

information.⁵⁰ Empirical studies have also shown that both physical and psychological benefits accrue to a patient who participates in treatment via an informed consent relationship with a health care professional.⁵¹

DTC genetic tests pose a potential threat to the established model of informed consent.⁵² A typical DTC “patient” orders the genetic test from a website. Although most companies offering DTC genetic tests include detailed information about the testing process on their websites, this information is not a substitute for a conversation with a health care professional about risks and benefits. Not surprisingly, the content of these websites is written to persuade as well as to inform; although the benefits of undergoing a test are highly touted, there is seldom any mention of risk.⁵³ Also notably missing from the content of these sites is information related to the alternatives of either obtaining a genetic test from a health care provider, or foregoing the test altogether.⁵⁴ Finally, in some unfortunate cases, the information provided on these websites may be deliberately misleading.⁵⁵

Proponents of DTC genetic tests may argue that the risks of undergoing these tests are minimal and thus the information obtained via a company’s website is sufficient to make an informed decision. As will be discussed, however, potential emotional and physical harms can result either directly from test results, or indirectly through patient misinterpretation or misuse of

⁵⁰ Andrews, *supra* note 46.

⁵¹ *Id.*

⁵² Novick, *supra* note 8, at 636.

⁵³ For example, the genetic testing service deCodeme’s website exclaims the health benefits of using its service and prominently includes patient testimonials on its webpage; the only disclaimer is found at the very bottom of the page in 8-point font of an almost illegible light grey against a white background. It states that deCodeme is for informational purposes only and “should NOT be used for medical decision making without consulting your physician.” deCodeme.com, Genes and Health, <http://www.decodeme.com/genes-and-health>.

⁵⁴ Of the major testing companies 23andMe, deCodeme, and Navigenics, there is no mention on the companies’ respective websites of the option of not testing.

⁵⁵ See Gregory Kutz, DIRECT TO CONSUMER GENETIC TESTS: MISLEADING TEST RESULTS ARE FURTHER COMPLICATED BY DECEPTIVE MARKETING AND OTHER QUESTIONABLE PRACTICES, GAO 10-847T, at 15 (2010).

results.⁵⁶ These risks are magnified when a patient does not consult with a health care professional in any stage of the testing process.⁵⁷

Some of the leading DTC genetic testing companies do offer over-the-phone (or over-the-web) genetic counseling services; however, this is insufficient as a mechanism for true informed consent for a variety of reasons.⁵⁸ First, the counseling is often not mandatory.⁵⁹ Given that many of the consumers of DTC genetic testing services may be those who have particularly strong privacy or autonomy concerns,⁶⁰ it is likely that a majority of these consumers will choose not to discuss their personal medical concerns with a counselor. Second, incentives offered to consumers by the companies with regard to counseling services might disrupt the informed consent process.⁶¹ For example, the popular DTC genetic testing company 23andMe offers free genetic counseling services only *after* a patient has purchased access to the test.⁶² When trying to decide whether or not to test, this is clearly unhelpful to a consumer. Finally, when a company does offer genetic counseling services prior to testing, these services may be tainted by the same bias towards testing that is evidenced on the company's websites.⁶³ Although potentially biasing financial incentives exist in any patient-provider relationship, these incentives are more troubling when unbuffered (unlike in most healthcare situations) by insurance and other intermediaries.⁶⁴

2. Accuracy and utility concerns

⁵⁶ See, e.g., Alberto Gutierrez, FDA official, Interview with the *New York Times*, (http://www.nytimes.com/2010/06/12/health/12genome.html?_r=1&scp=1&sq=gutierrez%20FDA%20genetic%20testing&st=cse) (June 11, 2010).

⁵⁷ *Id.*

⁵⁸ Novick, *supra* note 8, at 635-40.

⁵⁹ None of the three major genetic testing services companies (23andMe deCodeme and Navigenics) requires mandatory genetic counseling, although they all offer these services to varying degrees.

⁶⁰ See *supra* page 18, the discussion of the potential benefits of home genetic testing.

⁶¹ Novick, *supra* note 8, at 635-40.

⁶² 23andMe.com, 23andMe Enlists Informed Medical Decisions to Make Independent Genetic Counseling Services Available to Customers, <https://www.23andme.com/about/press/20100603/>.

⁶³ Novick, *supra* note 8, at 640.

⁶⁴ *Id.*

a. Clinical effectiveness and accuracy

Once a patient decides to proceed with a genetic test, concerns of test accuracy and clinical usefulness move to the forefront. These concerns are especially apparent with health-based tests purporting to provide “predictive” information about individual disease risk, and inhere from the probabilistic nature of risk prediction for polygenic diseases.⁶⁵ Scientists have reached a general consensus that current known associations between a given SNP and a given disease are generally so attenuated that they provide little useful predictive information.⁶⁶ For example, a 2008 paper in *Science* evaluating the usefulness of the type of studies relied on by DTC genetic testing companies (referred to in the paper as genome-wide association studies, or GWAS) found that “variants so far identified by GWASs together explain only a small fraction of the overall inherited risk of each disease (for example, ~10% of the variance for Crohn’s [Disease] and ~5% for [Type 2 Diabetes]). The primary value of [these associations] is not risk prediction, but providing novel insights about mechanisms of disease.”⁶⁷ Although the authors did not completely dismiss the future clinical utility of predictive genetic tests, they determined that “the extent to which genetic information will figure in ‘personalized medicine’ will depend on whether predictive accuracy beyond conventional measures can be attained, and whether there are interventions whose effectiveness is improved by knowledge of a genetic test.”⁶⁸ Similarly, the author of a review article in the *New England Journal of Medicine* explained that “what is becoming clear from these early attempts at genetically based risk assessment is that currently known variants explain too little about the risk of disease occurrence to be of clinically useful

⁶⁵ See, e.g., David Altshuter et al., *Genetic Mapping in Human Disease*, 322 SCIENCE 881, 881 (2008).

⁶⁶ *Id.*

⁶⁷ *Id.* at 885, 886.

⁶⁸ *Id.* at 887.

predictive value.”⁶⁹ The author of this article came to the conclusion that “patients inquiring about [GWAS] testing should be advised that at present the results of such testing have no value in predicting risk and are not clinically [useful].”⁷⁰ Thus, those most acquainted with the science agree that although predictive testing may play a future role in medicine, the science has not yet evolved to the point where the kinds of information that DTC genetic testing services are purporting to offer can be reliably obtained and usefully applied.

b. The importance of external factors in predicting disease

Because DTC genetic tests are focused on predicting risk for polygenic diseases, which result from a number of unknown environmental and genetic factors in addition to the genetic association identified and relied upon by the testing service, personal context is extremely important in interpreting test results.⁷¹ In many cases, this external contextual information is an even better predictor of disease than the association relied upon by the testing service. For example 23andMe offers a test for genetic susceptibility to lung cancer, although it is well known that the degree of risk for lung cancer attributable to genetic factors is dwarfed by the risk introduced by a patient’s status as a smoker or non-smoker.⁷² Family history of disease also often provides a better prediction of susceptibility to a given disease.⁷³ A DTC genetic test can be misleading insofar as it does not evaluate or report to the consumer (and in some cases the testers may not even be aware of the nature of) relevant external information that may have a much greater impact on an individual’s susceptibility to disease.

⁶⁹ Teri A. Manolio, *Genomewide Association Studies and Assessment of the Risk of Disease*, 363 NEW ENG. J. MED. 166, 173 (2010).

⁷⁰ *Id.* at 173-74.

⁷¹ Carla G. van El & Martina C. Cornel, *Genetic Testing and Common Disorders in a Public Health Framework: Recommendations of the European Society of Human Genetics*, 176 EU. J. HUM. GENETICS 1, 3 (2011).

⁷² Although 23andMe’s website makes clear that smoker status is the best predictor of lung cancer, similar situations could arise in which research has not yet revealed external risk factors whose predictive value is significantly greater than known genetic contributors.

⁷³ Van El & Cornel, *supra* note 70.

c. Effects of ethnicity and other factors on test validity

Even to the extent that the numbers provided by DTC genetic health tests have meaning, the meaning is limited to those whose ethnicity, approximate age, and gender match the underlying populations (usually white, middle aged men) on which the association studies are based.⁷⁴ The findings of these studies are heavily dependent on such factors.⁷⁵ Although some of the DTC testing companies' websites mention this caveat, they do not explicitly state that their tests are not recommended for certain populations, although for these groups most of the test results may be essentially meaningless.⁷⁶

d. Intra-industry variation in test results

These fundamental concerns about the predictive value of DTC genetic tests are exacerbated by intra-industry variation in test results.⁷⁷ The Government Accountability Office (GAO) released a report on DTC genetic testing services on July 22, 2010.⁷⁸ Among its findings, the report determined that there was a lack of standardization of test results among companies.⁷⁹ In other words, an individual testing with two different companies might be told that he is at increased risk for a particular disease by one testing company and that he is at decreased risk for the same disease by another testing company.⁸⁰ The report also cited potentially even more troubling concerns in the DTC genetic testing industry, including deceptive marketing practices and

⁷⁴ David Altshuter et al., *supra* note 64, at 884.

⁷⁵ *Id.*

⁷⁶ Of the major testing companies 23andMe, deCodeme, and Navigenics, only 23andMe mentions ethnicity. It does so in the context of specific tests. For example, it states on the prostate cancer information page that because a study including Japanese Americans was inconclusive, "the exact association in populations with Asian ancestry still needs to be confirmed." Presumably, this was only mentioned because a study in Asian Americans was in fact performed. There is no mention of ethnicity for other studies performed in only a single ethnic group. 23andMe.com, Prostate Cancer Sample Report, <https://www.23andme.com/health/Prostate-Cancer/>.

⁷⁷ Gregory Kutz, *supra* note 54, at 5.

⁷⁸ *Id.*

⁷⁹ *Id.*

⁸⁰ Justin P. Annes et al., *supra* note 5, at 1100.

erroneous medical management advice.⁸¹ These considerations further undermine the potential utility of such tests.

e. The possibility of conflicting recommendations

Finally, scientists worry that the nature of the DTC predictive tests currently being offered, which screen for predisposition to many conditions at a single time, might result in conflicting recommendations that are confusing or even dangerous to a consumer.⁸² For example, a nutrigenetic/predictive test might reveal that a consumer is predisposed both to osteoarthritis and Type II Diabetes. The consumer might of her own volition or upon the recommendation of the testing company decide to begin taking Glucosamine, a nutritional supplement that has been reported to help prevent and ease the symptoms of osteoarthritis.⁸³ However, Glucosamine may affect insulin sensitivity in certain populations, potentially exacerbating diabetic symptoms or precipitating the onset of diabetes.⁸⁴ DTC genetic testing companies are currently unprepared to deal with such potential complexities arising from the testing process.⁸⁵

3. Patient interpretation and use of results

Even if a consumer could be assured of receiving accurate, consistent, and non-misleading information from a DTC genetic testing service, a proposition that has been seriously questioned in the previous section, there remain health concerns arising from the patient's interpretation and use of such results.

a. Patient interpretation

⁸¹ Gregory Kutz, *supra* note 54, at 15.

⁸² Teri A. Manolio, *supra* note 68, at 173.

⁸³ McAlindon T.E. et al., *Glucosamine and Chondroitin for Treatment of Osteoarthritis: a Systematic Quality Assessment and Meta-Analysis*, 283 J. AM. MED. ASS'N, 1469 (2000).

⁸⁴ Joseph G. Yu et al., *The Effect of Oral Glucosamine Sulfate on Insulin Sensitivity in Human Subjects*, 26 Diabetes Care 1941 (2003). This study found that insulin sensitivity was reduced in obese patients, although it did not find an effect in overall populations.

⁸⁵ Teri A. Manolio, *supra* note 68, at 173.

First, the very nature of these tests gives rise to a problem of consumer interpretation. As previously discussed, these tests rely on association studies linking particular SNPs to incidence of a particular trait (such as disease or reaction to a drug) in the general population. The results of these studies yield a very specific type of statistical information that has meaning for researchers in the field, but may be meaningless (or at the very least difficult to understand and interpret) for an individual consumer.⁸⁶ That is not to say that consumers could not or should not be educated in the nuances of statistics and thus learn to interpret their test results in a sophisticated manner. However, when these problems of interpretation are combined with the accuracy problems outlined above, we may question whether it is worth undertaking this educational effort when the end result will be sophisticated interpretation of results that have little value in the first instance. In the meantime, misinterpretation or misuse of results could lead to serious concerns.

b. Psychological response to test results

One of these concerns is that consumers may be emotionally devastated by test results, and will lack the resources in a home testing environment to obtain appropriate psychological support. This argument is intimately related to the issue of informed consent.⁸⁷ Recent research, however, suggests that this particular concern may be unfounded.⁸⁸ An empirical study performed by Cinnamon Bloss and colleagues and reported in the *New England Journal of Medicine* found that consumers undergoing DTC genetic testing did not score significantly higher on stress-related indicators upon learning that they were at increased risk for a particular

⁸⁶ David Altshuter et al., *supra* note 64.

⁸⁷ Novick, *supra* note 8, at 636.

⁸⁸ Cinnamon S. Bloss et al., *Effect of Direct-to-Consumer Genomewide Profiling to Assess Disease Risk*, 364 NEW ENG. J. MED. 524 (2011).

disease such as heart disease or cancer.⁸⁹ The study does suggest, however, that these results may be partly attributed to the sample utilized in the study, since subjects who completed the study were self-selecting to some degree and likely had an above-average understanding of genetic testing.⁹⁰ Continued empirical research will be helpful in gauging the extent to which DTC genetic testing raises concerns about psychological harm resulting from adverse test results.

c. Patient action in response to test results

Perhaps more pressing than the concern that consumers will be devastated by adverse information related to their health is the concern that consumers will be falsely reassured by positive information. A finding of “no increased risk” certainly does not mean that a consumer exhibits zero risk for contracting a disease, especially since environmental and untested genetic factors may play an even greater role in disease onset than the tested marker. However, a consumer may psychologically rely on such information and may undergo increased psychic trauma if he or she contracts the disease. Even more dangerous is the possibility that the patient will adversely change her behaviors in reliance upon such information.⁹¹ 23andMe, for example, tests patients for both increased risk of heroin addiction and immunity to HIV resistance.⁹² A result of “no increased risk” or “HIV resistant” may lead a patient to engage in risky behaviors such as drug use or unprotected sex out of a false sense of immunity from the dangers of addiction or infection.

Related to this concern is the concern with pharmacogenetic testing that a patient will use test results to make treatment and dosage decisions independent of consultation with a health

⁸⁹ *Id.*

⁹⁰ *Id.* at 531.

⁹¹ See, e.g., Alberto Gutierrez, FDA official, Interview with the *New York Times*, (http://www.nytimes.com/2010/06/12/health/12genome.html?_r=1&scp=1&sq=gutierrez%20FDA%20genetic%20testing&st=cse) (June 11, 2010).

⁹² 23andMe.com, Health Reports: Complete List, <https://www.23andme.com/health/all/>.

care professional. The testing service 23andMe offers predictive response information for 19 treatments and drugs, including predicted response to Hepatitis C treatment.⁹³ A consumer receiving a result that he has reduced chances of responding to such treatment may discontinue the treatment without consulting his physician. This is a particularly likely possibility given that the treatment entails uncomfortable side effects. Even when a relationship between predicted responsiveness to a drug and a specific genetic profile is well-established and has been found to be of clinical usefulness, such as that between Warfarin metabolism and a SNP on the CYP2C9 gene, dosage is a complex calculation that relies on factors such as patient weight and age, and is best performed by a physician.⁹⁴

This concern is more than just hypothetical. A recent study found that “40% of participants with genetic test results indicating increased risk for Alzheimer’s disease reported increasing their use of medications or vitamins, compared with 20% of those whose results did not indicate increased risk.”⁹⁵

4. Economic concerns

Perhaps less pressing than public health concerns, but equally deserving of attention, are the economic consequences in engaging in DTC genetic health testing, both for individual consumers and society as a whole.

a. Waste of consumer money

The GAO study that found serious problems with the accuracy and marketing of DTC genetic health tests concluded that such tests at worst constitute a risk to consumer health and at best are

⁹³ 23andMe.com, Health Reports: Complete List, <https://www.23andme.com/health/all/>.

⁹⁴ See, e.g., A.L. Maguire et al., *supra* note 42.

⁹⁵ S. Chao et al., *Health Behavior Changes After Genetic Risk Assessment for Alzheimer Disease: the REVEAL Study*, 22 ALZHEIMER DIS. ASSOC. DISORD. 94 (2008).

a waste of consumer money.⁹⁶ This is not merely a trivial concern, given that the cost of testing ranges from hundreds to thousands of dollars per consumer.⁹⁷

b. Effects on the healthcare system

A second economic concern expressed by health care professionals is that consumers undergoing DTC genetic health tests will subsequently unnecessarily undergo additional tests, screenings, and physician consultations, thereby taxing the scarce resources of the healthcare system.⁹⁸ For example, an individual discovering that she is at increased risk for breast cancer may demand additional mammograms not currently indicated for her demographic group. However, the *New England Journal of Medicine* study tracking individuals' stress responses to the results of genetic health tests found that individuals receiving genetic testing did not generally undergo more screenings or tests subsequent to receiving personalized risk information.⁹⁹ Further, it could be argued that such screenings might actually prove useful and save the healthcare system money in the long run by increasing detection among high-risk groups identified by genetic testing. Thus, it is unclear what the consequences of wide-spread use of genetic testing would be on the healthcare system as a whole.

c. Physician liability

Finally, doctors have expressed concern that widespread use of DTC genetic health tests might give rise to increased physician liability.¹⁰⁰ This could occur, for example, if a patient feels that a doctor did not respond appropriately to the patient's disclosure of test results (for example, by ordering further tests or screenings) and thus failed to meet the proper standard of care. This

⁹⁶ Gregory Kutz, *supra* note 54.

⁹⁷ 23andMe charges \$200 for their service, while deCodeMe charges \$2000. Navigenics does not include pricing information on its website.

⁹⁸ Teri A. Manolio, *supra* note 68, at 174.

⁹⁹ Cinnamon S. Bloss et al., *supra* note 87.

¹⁰⁰ Justin P. Annes et al., *supra* note 5, at 1101.

could occur although the doctor may not have the information necessary to appropriately interpret the genetic test results, or may have a better understanding of the limitations of such tests than the patient himself. For example, a doctor may place a patient on a particular regimen of Hepatitis C treatment although genetic tests reveal that the individual may not respond optimally to such treatment because the doctor is also considering other information such as age, weight, the severity of illness, and the availability of other treatments. Although genetic tests can potentially provide relevant information that may help a doctor come to an ultimate decision, great uncertainty for doctors would result if DTC genetic tests could be introduced to establish a standard of care, especially given the extreme limitations of the information provided by such tests.

B. Potential benefits of DTC genetic tests

1. Patient autonomy

One of the foremost arguments forwarded in support of health-based DTC genetic tests involves the promotion of patient autonomy.¹⁰¹ There has been a trend in recent years for patients to become increasingly involved in the promotion of their health in the areas of both diagnosis and treatment.¹⁰² Allowing consumers to access DTC genetic testing services independently of a physician is arguably simply the next step in encouraging patient engagement and participation in health care. However, this argument has serious flaws. First, in order for a patient to truly make an independent decision regarding his health, he must have sufficient unbiased information to make an informed decision, something I have argued is seriously lacking in the context of DTC genetic testing. Second, even to the extent that a patient exercises autonomy in choosing to undergo DTC genetic health testing, this autonomy is subsequently limited when the patient is

¹⁰¹ Novick, *supra* note 8, at 641.

¹⁰² *Id.*

unable, due to a lack of appropriate information, context, and sufficiently predictive results, to make informed treatment decisions based on the results of such testing.¹⁰³

Although DTC genetic testing may not provide meaningful opportunity for autonomous decision-making in the realm of medical treatment, it can be argued that such testing may nevertheless encourage individuals to adopt healthier lifestyles so as to minimize the risks of contracting a particular disease. Such a result would indeed grant patients an opportunity for autonomy in making lifestyle decisions, and would also accrue benefits to society as a whole, reducing health care costs through preventative action and increasing the overall health and well-being of those who respond to the tests in this way. The empirical study performed by Bloss and colleagues, however, found that individuals undergoing DTC genetic health testing and finding themselves to be at risk for a particular disease (such as heart disease) generally did not respond by implementing healthy and appropriate lifestyle changes.¹⁰⁴ An important exception to this surprising result was found for those who discussed their test results with a doctor: these individuals did in fact implement healthy lifestyle changes.¹⁰⁵ Although it cannot be ruled out that individuals in this subgroup were generally more health-motivated overall (and thus were more likely both to talk to their physician and to implement healthy lifestyle changes), this finding generally supports the idea that autonomy may mean little without appropriate context and guidance.

Even if a patient were in a position to independently choose appropriate medical or lifestyle interventions upon receiving his test results, it is not clear that such interventions are available.¹⁰⁶ For example, in many cases doctors are uncertain as to the appropriate intervention

¹⁰³ *Id.*

¹⁰⁴ Cinnamon S. Bloss et al., *supra* note 87 at 529.

¹⁰⁵ *Id.* at 531.

¹⁰⁶ Carla G. van El & Martina C. Cornel, *supra* note 70.

for slightly increased risk of a disease as opposed to greater risk or onset of the disease itself.¹⁰⁷

Further, in some cases there are no medically accepted preventative measures to take, even for those who are almost certain of contracting a disease (this is the case with both Alzheimer's disease and Huntington's disease, for example).¹⁰⁸ A patient might be unduly distressed to learn that although she is at increased risk for a disease, there is nothing she can do about it.

2. Genetic privacy

An argument often forwarded by proponents of DTC genetic testing and related to the issue of patient autonomy is the argument that DTC genetic tests provide the opportunity for increased privacy and control over an individual's personal genetic information.¹⁰⁹ Such a view reflects concerns, arising with the sequencing of the human genome, that an individual's personal genetic information might be used by insurance companies, employers, the government, and others, without the permission and to the detriment of the individual.¹¹⁰ Such concerns are valid, and have provoked the response of the federal government. In 1995, former President Bill Clinton issued an executive order prohibiting the federal government from using personal genetic information for employment purposes.¹¹¹ This order did not extend to private employers, but many states subsequently enacted similar legislation that in some cases extended the reach of the executive order to insurance companies.¹¹² Further, in 2008, former President George W. Bush signed the Genetic Information Nondiscrimination Act (GINA).¹¹³ GINA provides for more comprehensive federal protection of genetic information, and includes prohibitions on the use of

¹⁰⁷ *Id.*

¹⁰⁸ *Id.*

¹⁰⁹ Novick, *supra* note 8, at 641.

¹¹⁰ *Id.*

¹¹¹ National Human Genome Research Institute, Genetic Discrimination Fact Sheet, <http://www.genome.gov/10002328>.

¹¹² *Id.*

¹¹³ National Human Genome Research Institute, Genetic Information Nondiscrimination Act of 2008, <http://www.genome.gov/10002328#3>.

genetic information by private employers in making employment decisions and health insurance companies in making decisions to raise individual premiums or deny benefits.¹¹⁴ This legislation still contains some gaps (for example, it does not cover life insurance or disability insurance), and some have exhibited concerns about enforcement, but generally the reaction of concerned groups to the enactment of GINA has been positive.¹¹⁵

Although GINA clearly does not address all the concerns of those who worry about privacy of genetic information, to the extent that GINA addresses these concerns, the subsequent need to turn to home genetic testing as a self-help measure is thereby lessened. Further, it is not clear that turning to DTC genetic testing fully solves the privacy problem either. Although the major DTC genetic testing companies reassure customers with promises of utmost privacy,¹¹⁶ it is not difficult to imagine situations in which this information might be inadvertently or intentionally released to third parties. DTC genetic testing companies are not regulated entities under the comprehensive federal health care information privacy statute, HIPAA.¹¹⁷ Thus, they are not required by law to follow the rigorous guidelines governing protection and release of personal health information in other contexts. Further, it is unclear what will happen to this data if a company is sold, merges with another company, or is otherwise dissolved.¹¹⁸ Thus, the popular perception that genetic information is ‘safer’ or ‘more private’ in the hands of private companies than it is in the public health care system may well be baseless.

3. Ex ante effects on innovation

Finally, some who see the future potential in DTC genetic testing argue that overly stringent

¹¹⁴ *Id.*

¹¹⁵ Novick, *supra* note 8, at 641.

¹¹⁶ For example, the Navigenics website reassures customers with the rather disturbing statement that “unlike some other companies, we do not sell or share your genetic information.” Navigenics.com, What we Offer, http://www.navigenics.com/visitor/what_we_offer/.

¹¹⁷ See Health Insurance Portability & Accountability Act of 1996, 29 U.S.C.A. §1181 et. seq.

¹¹⁸ James P. Evans et al., *Preparing for a Consumer-Driven Genomic Age*, 363 NEW ENG. J. MED. 1099 (2010).

regulation of these tests would amount to an effective ban of the tests.¹¹⁹ In addition to eliminating the availability of such tests to those who choose them, such a result would also have the consequence of inhibiting product development and improvement.¹²⁰ This concern is particularly salient given that although scientists are doubtful about the current utility of DTC genetic tests, many concede that further scientific developments could lead to increased clinical usefulness.¹²¹ However, much of the scientific research on which the increased utility of the tests will rely is basic research that is likely to be performed not by the genetic companies themselves, but by government sponsored and university research labs.¹²² These companies already rely heavily on this type of independent research for the current utility of their tests, and it is doubtful that they will begin to undertake independent research to validate or improve the utility of their product unless required to do so by regulation. Further, if and when the science does advance to a point at which DTC genetic tests are deemed to be of clinical utility, it is important that the public's trust in such tests has not undermined by a long proliferation of testing products of doubtful utility.¹²³

C. Summary

Although it is currently unclear whether some of the concerns regarding DTC genetic testing (for example, concerns about economic effects on the healthcare system) are well-founded, other concerns, such as those regarding test accuracy and potential response of patients to test results, are clearly grounded in empirical research and pose pressing public health issues that should be addressed. Further, the potential benefits of DTC genetic testing, such as patient autonomy and

¹¹⁹ See, e.g., A.L. Maguire et al., *supra* note 42.

¹²⁰ *Id.*

¹²¹ See, e.g., David Altshuter et al., *supra* note 64.

¹²² The correlations between SNPs and health measures on which these tests rely are all performed by outside parties. Further, the DNA chip on which these services rely is a technology that was first developed and used by researchers in a Medical College. Leonard H. Augenlicht & D. Kobrin, *Cloning and Screening of Sequences Expressed in a Mouse Colon Tumor*, 42 *Cancer Research*, 1088–1093 (1982).

¹²³ Carla G. van El & Martina C. Cornel, *supra* note 70.

patient privacy, are subject to important caveats. The clearest benefit of such testing, ex ante product development, would likely not be greatly harmed by increased regulation, since the current and future utility of these products depends heavily on outside research.

IV. Current regulation of DTC genetic tests

Given the important and serious health and safety concerns with DTC genetic tests, the current regulatory landscape for these tests is inadequate. This landscape is filled with grey areas and uncertainty. Several entities currently have jurisdiction to regulate genetic testing, and yet DTC genetic health testing has until recently largely slipped through the cracks of these overlapping jurisdictions.¹²⁴ Only recently has the FDA begun asserting increased control over the producers and marketers of DTC genetic tests.¹²⁵

A. CLIA regulation

The Clinical Laboratory Improvement Amendments (CLIA) grant the Centers for Medicare and Medicaid Services (CMS) authority to regulate laboratory testing of human specimens for the diagnosis and/or treatment of disease, including genetic testing.¹²⁶ A laboratory wishing to perform such tests must thus obtain a federal certificate of approval before doing so.¹²⁷ Under this regulatory scheme, tests are classified into one of three categories: waived, moderate complexity, and high complexity.¹²⁸ Tests in the waived category are simple tests that have negligible likelihood of a false result and that pose no risk to the patient.¹²⁹ Moderate and high complexity tests are ranked according to a set of criteria that includes the degree of technical

¹²⁴ Novick, *supra* note 8, at 623.

¹²⁵ In September 2010, FDA sent letters to five DTC genetic testing companies, requesting that these companies submit premarket approval applications for their products. See FDA.gov, Medical Devices Letters to Industry, <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/ucm111104.htm>.

¹²⁶ Ctrs. for Medicare & Medicaid Servs., CMS Initiatives to Improve Quality of Lab. Testing under the CLIA Program 1 (2006), available at <http://www.cms.hhs.gov/CLIA/downloads/060630.Backgrounder.rLEG.pdf>.

¹²⁷ *Id.*

¹²⁸ 42 C.F.R. § 493.5 (2007).

¹²⁹ 42 C.F.R. § 493.15 (2007).

knowledge and individual judgment required to perform the test and reliability of results.

Genetic tests thus qualify as “high complexity” tests.¹³⁰

Although classified as a high complexity test, genetic testing is not subject to all of the stringent proficiency requirements required of other high and moderate complexity tests.¹³¹

Generally, moderate and high complexity tests must follow quality assurance programs and undergo proficiency testing.¹³² Proficiency testing, in turn, is based on a categorization system of specialties and subspecialties of scientific expertise, each with its own proficiency standards to which a lab seeking certification in that area must comply.¹³³ The proficiency testing assures the accuracy of the test and imposes other requirements specific to that specialty. However, there is no subspecialty for genetic testing under CLIA.¹³⁴ In the event that a relevant subspecialty does not exist, such as for genetic testing, there are no specific proficiency standards to which a lab must adhere.¹³⁵ Instead, the lab in question is required to “establish and maintain the accuracy of its testing procedures,” and may do so in a variety of ways; for example, by conducting its own statistical tests of patient results or comparing its test results with another lab.¹³⁶ For several years, various groups have lobbied for the addition to CLIA of a subspecialty for genetic testing in an effort to standardize and improve proficiency requirements for the genetic testing industry.¹³⁷ However, thus far, such efforts have been to no avail.

The creation of a genetic subspecialty under CLIA would doubtless improve the regulatory environment for genetic testing; however, it is noteworthy that CLIA (whatever

¹³⁰ See Am. Soc’y of Human Genetics Bd. of Dirs., *ASHG Statement on Direct-to-Consumer Genetic Testing in the United States*, 81 Am. J. Human Genetics 635, 636 (2007), available at http://www.dnapolicy.org/resources/ASHG_DTC_statement.pdf.

¹³¹ Novick, *supra* note 8, at 625.

¹³² 42 C.F.R. § 493.801 (2007).

¹³³ Novick, *supra* note 8, at 625.

¹³⁴ *Id.*

¹³⁵ *Id.*

¹³⁶ 42 C.F.R. § 493.801(a)(2)(ii).

¹³⁷ Novick, *supra* note 8, at 626.

standards it imposes) addresses only the accuracy and not the clinical validity of tests. Thus, it does not address situations, often encountered in DTC genetic health tests, where a test may be performed correctly, but the results themselves are misleading. This could occur, for example, if a test is based on weak association data or is valid only for a specific ethnic group.

B. FTC regulation

The Federal Trade Commission (FTC), which regulates food and drug advertising, has jurisdiction over the advertising of DTC genetic tests. Although it has acknowledged this jurisdiction, the FTC has not at present regulated the marketing of DTC genetic health testing.¹³⁸ The FTC did, however, release a notice to consumers in 2006 stating its concerns with DTC genetic tests and recommending that consumers do not use these tests unless under the supervision of a doctor.¹³⁹

C. State regulation

Local regulation of genetic testing services, and DTC genetic testing services in particular, varies from state to state.¹⁴⁰ For general genetic testing services, only two states have implemented standards that are more stringent than the federal CLIA standards.¹⁴¹ DTC genetic tests have been regulated more stringently, with several states either banning their use outright, or requiring

¹³⁸ *Id.* at 629.

¹³⁹ Federal Trade Commission, FTC Facts for Consumers, At-Home Genetic Tests: A Healthy Dose of Skepticism May Be the Best Prescription 1 (July 2006), <http://www.ftc.gov/bcp/edu/pubs/consumer/health/hea02.pdf>.

¹⁴⁰ Novick, *supra* note 8, at 630.

¹⁴¹ Centers for Medicare and Medicaid Services, *CMS Initiatives to Improve Quality of Laboratory Testing Under the CLIA Program 2* (July 2006), <http://www.cms.hhs.gov/CLIA/downloads/060630.Backgrounder.rLEG.pdf>; Centers for Medicare and Medicaid Services, List of Exempt States Under the Clinical Laboratory Improvement Amendments (CLIA), <http://www.cms.hhs.gov/CLIA/downloads/Exempt.States.List.pdf>.

a prescription for their use.¹⁴² However, because most of these tests are marketed online, enforcement of these local regulations poses a problem.¹⁴³

D. FDA regulation

FDA has jurisdiction under the 1976 Medical Device Amendments to the Food, Drug and Cosmetic Act to regulate genetic tests as medical devices, and, more specifically, in vitro diagnostic devices (IVDs).¹⁴⁴ The steps with which a medical device company must comply before offering the device to the public vary with the FDA's classification of the device.¹⁴⁵ Class I devices are classified as low-risk and are subject to the least amount of regulation.¹⁴⁶ Class II devices are classified as higher-risk and must comply with premarket notification (510(k)) procedures as well as being subject to additional controls to assure safety and effectiveness.¹⁴⁷ Class III devices, classified as highest-risk, must usually undergo a rigorous premarket approval process in which clinical data are submitted to the FDA to demonstrate both the safety and effectiveness of the product.¹⁴⁸

1. The laboratory-developed test exception

¹⁴² Gail H. Javitt, Erica Stanley & Kathy Hudson, *Direct-to-Consumer Genetic Tests, Government Oversight, and the First Amendment: What the Government Can (and Can't) Do to Protect the Public's Health*, 57 OKLA. L. REV. 251, 258 (2004).

¹⁴³ For example, although DTC genetic tests are banned in some states, the genetic testing service Navigenics makes no mention on their website of these state restrictions. Navigenics.com, <http://www.navigenics.com/>. In its Terms of Service, 23andMe places the burden on the customer by stating that an agreement to the Terms of Service includes a representation that “you are [not] a person barred from receiving the Services under the laws of the jurisdiction in which you are resident or from which you use the Services.” 23andMe.com, Terms of Service, <https://www.23andme.com/about/tos/>. Only deCodeMe explains that it will omit certain genetic information for customers in states where dissemination of this information is illegal; however, this information is buried in the fine print and customers in these states will likely be surprised when they do not receive full testing information. deCodeMe.com, deCodeMe Genetic Scan Service Agreement and Informed Consent, <http://www.decodeme.com/service-agreement>.

¹⁴⁴ Steve Gutman, *The Role of Food and Drug Administration Regulation of In Vitro Diagnostic Devices—Applications to Genetics Testing*, 45:5 CLIN. CHEM. 746 (1999).

¹⁴⁵ See 21 U.S.C.A. §360.

¹⁴⁶ See *id.* at §360(a)(A)(i).

¹⁴⁷ See *id.* at §360(a)(B)(ii).

¹⁴⁸ See *id.* at §360(a)(C)(ii).

Because the clinical effectiveness of many DTC genetic tests has not been established, these tests would at least initially be classified as Class III devices and would thus be subject to a rigorous premarket approval process.¹⁴⁹ However, DTC genetic tests on the market today have avoided this process because of the “home brew” or laboratory- developed test (LTD) exception for IVDs.¹⁵⁰ LTDs include tests that are developed in-house by the company offering the testing service, rather than those that are marketed to several labs.¹⁵¹ Because most DTC genetic testing services do indeed develop their own tests, this exception is relevant. FDA has historically exercised its discretion to exempt LTDs from premarket approval, due in part to resource constraints, but also due in part to FDA’s opinion that LTDs were generally “relatively simple, well-understood tests that diagnosed rare diseases and conditions, and that were intended to be used by physicians and pathologists in a single institution where they were actively involved in patient care.”¹⁵² Although this is true of many LTDs, it is not true of DTC predictive genetic tests that are intended to be used independently by consumers and that evaluate propensity to develop a wide variety of relatively common diseases.

In 1998, FDA increased regulatory oversight of LTDs somewhat by promulgating a regulation imposing minimal requirements on LTDs with active analyte specific reagents (ASRs).¹⁵³ In the process of promulgating this regulation FDA considered requiring heightened

¹⁴⁹ Anny Huang, *FDA Regulation of Genetic Testing: Institutional Reluctance and Public Guardianship*, 53 FOOD & DRUG L.J. 555, 562 (1998).

¹⁵⁰ See Gutman, *supra* note 142, at 746.

¹⁵¹ *Id.*

¹⁵² COUNCIL FOR RESPONSIBLE GENETICS, FDA INVESTIGATION INTO DIRECT TO CONSUMER GENETIC TESTING COMPANIES: AN ANALYSIS (2010).

¹⁵³ Gutman, *supra* note 142, at 746. The active ingredients of DTC genetic tests fall within FDA’s definition of ASRs, which includes “antibodies, both polyclonal and monoclonal, specific receptor proteins, ligands, nucleic acid sequences, and similar reagents which, through specific binding or chemical reactions with substances in a specimen, are intended for use in a diagnostic application for identification and quantification of an individual chemical substance or ligand in biological specimens.” 21 CFR 864.4020(a).

scrutiny for predictive genetic home brew ASR tests; however, they did not do so.¹⁵⁴ The ASR regulation exempts LTDs from premarket notification and premarket approval requirements, but subjects the test ingredients to general quality controls and labeling requirements.¹⁵⁵ Although the ASR regulation helps assure the quality of the product used, it, like the CLIA regulations, does not address the clinical effectiveness of the test, or the safety concerns arising from the release of tests results to the public.

2. Recent FDA action with respect to DTC genetic testing services

In June 2010, FDA demonstrated its intention to discontinue its practice of exempting DTC genetic test from premarket approval as LTDs. It did so by sending letters to five DTC genetic testing companies.¹⁵⁶ The letters requested that these companies submit premarket approval applications to FDA, suggesting that FDA does indeed consider these tests to be Class III devices.¹⁵⁷ Further, some of the letters stated that FDA does not consider the DTC genetic tests at issue to be LTDs because “the [tests are] not developed by and used in a single laboratory.”¹⁵⁸ Although two of the five letters sent by the FDA do not include the statement that FDA does not consider the test at issue to be an LTD, the fact that these companies nevertheless received a letter suggests that FDA may be considering excluding all DTC genetic tests from the LTD exemption, regardless of their definitional status as an LTD.¹⁵⁹ This move by FDA would allow for the most comprehensive regulation to date of DTC genetic tests.

V. Conclusion: FDA’s role in the future of DTC genetic test regulation

¹⁵⁴ Medical Devices; Classification/Reclassification; Restricted Devices; Analyte Specific Reagents, 62 Fed. Reg. 62,243 (Nov. 1997).

¹⁵⁵ See, e.g., 21 CFR 807.20(a) (requiring registration of devices); 21 CFR 809.10(e) (specifying labeling requirements); 21 CFR 809.30 (restricting the sale and use of ASR tests but not test results).

¹⁵⁶ See FDA.gov, Medical Devices Letters to Industry, <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/ucm111104.htm>. The five companies included Knome, Inc., 23andMe, Inc., deCode Genetics, Illumina, Inc., and Navigenics.

¹⁵⁷ COUNCIL FOR RESPONSIBLE GENETICS, *supra* note 150.

¹⁵⁸ FDA.gov, Medical Devices Letters to Industry, *supra* note 154.

¹⁵⁹ COUNCIL FOR RESPONSIBLE GENETICS, *supra* note 150.

Given the potential dangers and problems with current DTC genetic testing services, it is clear that more stringent and consistent regulation is required to ensure that the products reaching the market are safe, effective, and yield accurate results that can be safely and properly used by consumers. However, many of the potential avenues for regulating DTC genetic testing services are either inadequate or pose difficult implementation and enforcement challenges. CLIA regulation currently does not have sufficiently specific or consistent proficiency standards for genetic testing due to the lack of a genetics subspecialty; more importantly, CLIA regulation does not address the clinical effectiveness of laboratory tests.¹⁶⁰ FTC regulation may regulate the claims made by DTC genetic testing services in advertising, but lacks jurisdiction to engage in more substantive regulation of the safety and effectiveness of the products.¹⁶¹ Finally, state regulation lacks consistency and is difficult to enforce given that most providers of DTC genetic testing services sell their products over the internet.¹⁶²

Because of the inadequacy of or challenges posed by these regulatory schemes, FDA regulation shows the most potential for providing a comprehensive and consistent regulatory environment for DTC genetic testing services. Medical device regulation under the Food, Drug and Cosmetic Act allows FDA to require premarket approval for the demonstration of safety and effectiveness where necessary, but also allows for flexibility via the medical device classification system. Thus, if FDA chooses to classify a specific lower-risk genetic test as Class I or Class II, full premarket approval would not be required for that test.¹⁶³ For example, FDA official Alberto Gutierrez told the public media that a genetic test for baldness would in all likelihood be

¹⁶⁰ 42 C.F.R. § 493.801 (2007).

¹⁶¹ See Genetics and Public Policy Center, Direct-to-Consumer Genetic Testing: Empowering or Endangering the Public? (July 25, 2006), <http://www.dnapolicy.org/policy/issue.php?action=detail&issuebriefid=32>.

¹⁶² Novick, *supra* note 8, at 631.

¹⁶³ See 21 U.S.C.A. §360.

classified as a Class I medical device not requiring premarket approval.¹⁶⁴ Further, as the safety and effectiveness of Class III DTC genetic tests are established, these tests can be down-classified to Class II devices, allowing future marketers of these products to obtain approval simply by showing that their test is substantially similar to an approved test under 510(k) review.¹⁶⁵ This regulatory approach strikes the proper balance of regulation for genetic testing services that pose real risks to the public, while allowing for innovation and improvement in the genetic testing market by imposing less stringent regulation on safer tests.

Eight years following the sequencing of the human genome project, and after many years of uncertainty in the regulation of DTC genetic test, FDA has taken the right approach by beginning to exercise jurisdiction over genetic testing services as Class III devices, and should continue to move down this path. Courts should also construe the Food, Drug and Cosmetic Act and the Medical Device Amendments so as to ensure that FDA may continue to exercise jurisdiction over DTC genetic testing companies. In particular, DTC genetic tests should be considered as IVD medical devices under the jurisdiction of FDA and not falling under the LDT or other exemption.¹⁶⁶ This approach will help ensure that the public has access to safe and effective genetic testing products and that the important policy and public health issues created by DTC genetic testing are properly addressed.

¹⁶⁴ Alberto Gutierrez, interview with the *New York Times*, *supra* note 90.

¹⁶⁵ See 21 U.S.C.A. §360(a)(B)(ii).

¹⁶⁶ Another possible exemption which DTC genetic testing services could exploit is the Investigational Device Exemption (IDE). This exemption allows a device to be experimentally tested without undergoing premarket approval. However, since such an exemption requires submission of a request to the FDA, and DTC genetic testing services have not submitted such requests, it is unlikely that these companies will be able to claim this exemption. See COUNCIL FOR RESPONSIBLE GENETICS, *supra* note 150.