The FDA and 23andMe:
Violating the First Amendment or Protecting the Rights of Consumers?

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One of the largest direct-to-consumer (DTC)2 genetic testing facilities, 23andMe, was ordered by the U.S. Food and Drug Administration (FDA) to cease marketing its Personal Genome Service (PGS) test on Nov. 22, 2013 (1). This occurred after 23andMe failed to respond to questions from the FDA about the analytical and clinical validity of this test (see Table 1 for definitions). In response to the FDA’s order, 23andMe no longer provides health-related genetic risk assessments but still provides the genetic data (i.e., genotypes) and ancestry-related genetic reports. Although some support the FDA’s actions because of the test’s potential for harm to consumers, other personalized medicine advocates are crying foul, saying that the FDA is being overly paternalistic and impeding medical advances. Green and Farahany, in a recent commentary in Nature, argued that the FDA’s actions are “unwarranted without evidence of harm” (2). They further stated that these types of FDA regulations are disallowing advertising (“commercial speech”) as well as preventing individuals from their right to receive information, both of which are protected under the First Amendment. The FDA might counter that this medical device is subject to all of the same regulations as all other medical devices.

Part of the complaint by some has been that the FDA should not presume that consumers are unable to understand their own genomic information and therefore deny consumers access to these data. However, in its personalized medicine document, the FDA states that its “mission is to protect and promote the health of all Americans through assuring the safety, efficacy, and security of drugs, biologics..., and medical devices.” In the case of medical products, FDA determines that products are safe and effective before marketing through a careful evaluation of benefits and risks that considers the available scientific data in the context of the underlying condition or disease” (3). They further say that stakeholders in personalized medicine need to consider analytical and clinical validity as well as clinical utility, which is essentially, how much value the test adds to patient care (3). Therefore, the FDA might say that its role is not to prevent consumers from receiving their own genomic information, but rather to protect consumers from receiving potentially invalid information.

Arguably, 23andMe have been revolutionary in their approach to provide genomic data directly to consumers, without the need for a physician to first order the test. Their $99 saliva-based DNA test, which tests for 254 “health conditions and traits,” could be considered a bargain considering that interrogation of genetic variants for each disorder individually would cost a great deal more than $99 if performed through traditional clinical care routes. Furthermore, 23andMe provided reports (before the FDA order) that contained lifetime risk calculations and references to studies linking tested genomic targets to specific conditions. However, there notably are several shortcomings to the PGS test that are not apparent to non-geneticists. First, 23andMe does not perform comprehensive genetic analyses for their tests. Their inherited disorders testing panel, which includes analyses for carrier status for >50 conditions, contains a large caveat in that it includes only a small percentage of possible pathogenic mutations (usually founder mutations present only in specific populations, and in general not accounting for much of that disease risk). For example, in its BRCA1 and BRCA2 analyses for hereditary breast and ovarian cancer, the PGS test looks for 3 mutations that are common in individuals of Ashkenazi Jewish descent, yet there are >2000 reported mutations in these genes. Non-Ashkenazi individuals who have no mutations identified may believe they are free from BRCA mutations when, in fact, this test has not begun to address their risk. These largely incomplete genetic tests for inherited disorders are of limited clinical value and could create misperceptions among consumers who are not aware of what is missing from the test.

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2 Nonstandard abbreviations: DTC, direct-to-consumer; FDA, US Food and Drug Administration; PGS, Personal Genome Service.
A second major shortcoming of the PGS test relates to unvalidated predictions of risk for the group of tests listed as “health risks.” These include >120 disorders of known polygenic/multifactorial etiology (for example, atrial fibrillation, celiac disease, and restless legs syndrome). Not apparent to the casual consumer of DTC testing is that for many disorders there may be a long list of known associated markers, but the current test only reads a handful of the markers. The DTC company then uses an unvalidated algorithm to provide a risk score. Although it is very satisfying to the consumer to have medical risks laid out in this black-and-white fashion, the results are highly suspect. This type of unvalidated analysis and incomplete testing is what has led to reports of individuals having testing at >1 DTC company and receiving highly disparate reports of their risks. This is hardly a surprise when one looks behind the curtain at how these risk scores are generated.

Each “health risk” reported in the PGS test is the probability that the individual being tested will develop a condition. This absolute risk is derived by use of an algorithm that calculates a value for the product of all of the relative risks of the genomic markers and then multiplies this value by the average population risk for the condition (4). One criticism of this model is that the final average lifetime risk is dependent on which variables (e.g., age, sex, ethnicity) are used to define “population.” Another criticism of this algorithm is the lack of weighting of risk on the basis of strong-effect vs. weak-effect genomic markers and odds ratios. Furthermore, it has been suggested that many of the genomic marker risk values are too small to be statistically valid and therefore should not be included (5). It is also noteworthy to point out that oftentimes, surrogate genetic markers are used instead of directly testing the actual risk marker, which may lead to false-positive or false-negative assumptions. Previous studies have demonstrated that these factors and more (e.g., definition of phenotype) have all contributed to large disparities in absolute risks reported by DTC genetic testing companies (4, 5).

So, why not let consumers simply take their own genomic data and health risk calculations and “change what they can and manage what they can’t” as per 23andMe? According to Green and Lahaney, the type of information provided by DTC companies such as 23andMe may only lead to transient anxiety, if any, in the consumer. Furthermore, they cite studies that most patients will not self-prescribe or change healthcare actions on the basis of their genomic data without first consulting a physician. Both are certainly good news, but critics are quick to point out that the majority of users of the DTC genomic tests are highly educated and have easy access to healthcare. Furthermore, consumers likely apply subjective interpretations of genetic risk data and may not fully understand the clinical validity or utility or limitations of their test results. Therefore, medical providers (the majority of them hardly any more prepared than the general consumer to understand these reports) then need to step in to help the consumers understand their genetic data and provide relevant follow-up such as confirmatory testing or other measures.

This discussion then transitions into the next major issue, which is the strains that this test places on the healthcare system because of increased resources required to educate medical providers to help them understand these unvalidated reports, and increased workload of medical providers to educate consumers about their test results. One study observed that 85% of primary care physicians did not feel prepared to answer patients’ questions on DTC testing (6). The majority of respondents to the study also had concerns about DTC testing leading to incorrect interpretation of results by patients, misleading advertisements, and questionable clinical utility. Another study found that 92% of genetic counselors perceived that patients were at risk of receiving misinformation from DTC tests, and 96% of them would not recommend DTC genetic testing to their patients (7).

In their argument, Green and Farahany state that consumers have the right to access their own genomic information. This may be true, but 23andMe was for the most part providing unvalidated risk calculations for a test that has many limitations and little clinical utility and therefore cannot be realistically considered “genomic information.” Furthermore, 23andMe has failed to respond to the FDA’s requests for proof of analytical and clinical validation. Therefore, the FDA

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**Table 1. Definitions of terms.**

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<tr>
<th>Term</th>
<th>Definition</th>
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<tr>
<td>Analytical validity</td>
<td>How well the test predicts the presence or absence of a particular gene or genetic change; in other words, whether the test can accurately detect whether a specific genetic variant is present or absent.</td>
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<tr>
<td>Clinical validity</td>
<td>How well the genetic variant being analyzed is related to the presence, absence, or risk of a specific disease.</td>
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<tr>
<td>Clinical utility</td>
<td>Whether the test can provide information about diagnosis, treatment, management, or prevention of a disease that will be helpful to a consumer.</td>
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*Source: National Library of Medicine (8).*
was left with no choice but to require that if 23andMe wants to sell a health-related medical device to consumers, it needs to demonstrate that its product is safe and effective or cease offering the test. DTC companies should have a sense of responsibility to provide tests that are only clinically valid (and further prove that the tests are analytically valid) and can be used in ways to provide information about diagnosis, treatment, management, or prevention of a disorder. Including a large group of incomplete and/or meaningless tests with unvalidated risk calculations confuses the consumer, demeans the overall test, and contributes to wasted healthcare time and money.

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References