The FDA vs. 23andMe: A Lesson for Health Care Entrepreneurs

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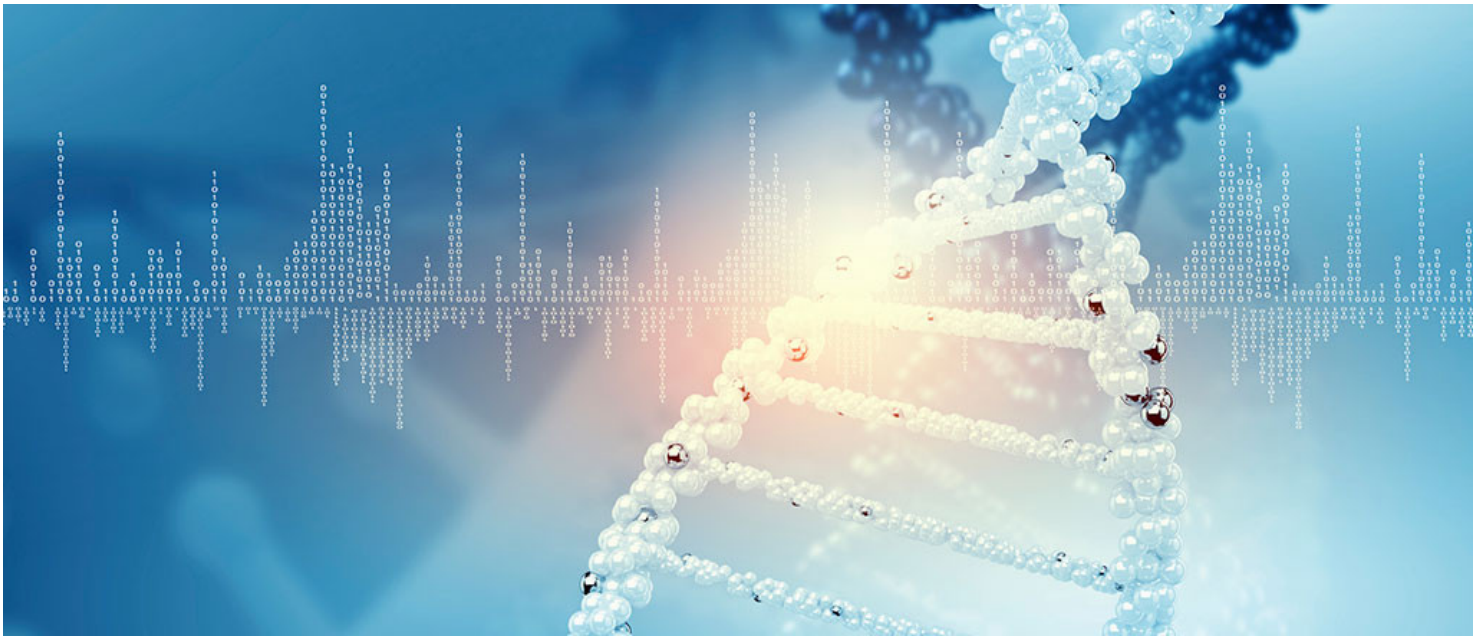
Innovation



When personal genomics and biotech firm 23andMe was founded in Mountain View, Calif., in 2006, the hype over the genetic tests it offered directly to consumers was immediate and irresistible to many. The company promised that for a nominal fee, it could scan your saliva sample and tell you — based on your genetics — everything from who your ancestors were to what diseases you may be at risk of developing many years down the road. 23andMe raised more than $100 million in capital from such big-name investors as Google and Genentech. Today, the company's website boasts having close to 500,000 "genotyped consumers."

So it was a surprise to some observers when, on November 22, the U.S. Food & Drug Administration (FDA) sent a strongly worded letter to 23andMe CEO Anne Wojcicki demanding that the company stop marketing its test, called Personal Genome Service (PGS), until it secures authorization from the agency. The FDA contends that PGS is a medical device being pitched for the diagnosis and prevention of disease, and therefore it must obtain approval under federal law.

Whenever regulators step in and try to yank a product off the market — particularly when the company selling it is already well entrenched — it invariably sparks a debate about whether over-regulation will stifle technology innovation. However, some experts believe the real issue at stake in the 23andMe controversy is not innovation, but rather the firm's selling strategy. "I suspect that a lot of this boils down to the way 23andMe has been marketing itself. It has taken a pretty aggressive stance in saying its services have a medical benefit," notes Reed Pyeritz, professor of medicine and chief of the division of medical genetics at the Perelman School of Medicine at the University of Pennsylvania. "That does get the attention of the FDA."

Indeed, as the FDA pointed out in its letter, PGS promised to provide information on 254 health conditions, including heart disease, diabetes and breast cancer. 23andMe offered complete reports along with the test results, with advice on genetic susceptibility, potential response to particular drugs and preventative steps customers might take to protect their health. "Most of the intended uses for PGS listed on your website, a list that has grown over time, are medical device uses," the warning letter says.

The understanding of the human genome is still in its infancy, and in most cases, genetic susceptibility to a disease does not translate into a definitive risk of developing that condition. The FDA expressed concern that 23andMe's customers would take drastic measures to prevent diseases without fully understanding what their genetic results truly prove about their risks. "The

worries are well-founded because who knows what individuals will do with information that they interpret themselves?" Pyeritz says. "Very few genetic tests actually have been studied for clinical utility. Had 23andMe been marketing things more truthfully, I wonder if they would have ever gotten this warning letter from the FDA."

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23andMe continues to sell PGS; however, it is only offering ancestry information and raw genetic data without any interpretation, a spokeswoman for the company told Knowledge@Wharton in an e-mail. "Our goal is to work with the FDA in a way that clearly demonstrates the benefit to people and the validity of the science that underlies the test," she wrote, adding that the company intends to "complete the regulatory review process."

'Recreational Genetics'

Just how useful are genetic tests marketed directly to consumers? Pyeritz has undertaken a few studies designed to answer that question. One set of studies, done in conjunction with the Coriell Institute for Medical Research in Camden, N.J., set out to determine the demographics of people who seek out direct-to-consumer genetic tests. The researchers discovered that most customers are Caucasian, well educated and economically upscale — exactly what they expected for a product that could be considered "recreational genetics," Pyeritz says.

"Beyond that, we asked them what they intended to do with the information," he notes. "The majority said, 'We're going to give it to our physicians.'"

So Pyeritz and his collaborators launched a subsequent study to examine how much physicians understand about genetics, and to determine how they might react when patients start marching in with maps of their genomes that they ordered themselves. "Most of the physicians said they didn't know what they were going to do with that kind of information," Pyeritz says. "The vast majority of them do order a genetic test occasionally, but it's a much more targeted test" for diseases that can be definitively linked to particular genes. "These are not the kinds of tests that 23andMe is offering."

Robert Field, a Wharton health care management lecturer, believes the 23andMe technology would not have generated so much regulatory concern if it had been marketed to doctors instead of consumers. "Any kind of genetic testing has to be combined with professional counseling to do the patient any real good," he notes. "The concern is that when you do a home test, you're not going to get that counseling, and you're not going to know how to act appropriately on the results." If the test had been marketed to doctors instead, Field adds, "you would have built into the process the professional advice needed."

However, genetic tests sold to doctors constitute an entirely different market — a considerably less sexy market, Field points out, and an unlikely departure for a company like 23andMe. "The point of 23andMe was to mass market an inexpensive test that people can do at home without the need to visit a physician. If you've got to go to your doctor, that negates the company's business model."

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According to Field, there's always a risk that regulatory actions such as the FDA's warning letter to 23andMe could dissuade other entrepreneurs from developing new genetic-testing technology, but any regulatory policy must always balance the need to encourage innovation with the need to protect the public. "One person's innovation is another person's quackery," he notes.

The Challenge of Validating Genes

One of the biggest problems with direct-to-consumer genetic tests is that they burden users with a lot of information that may or may not be relevant to their medical future, says Jason Karlawish, a professor of medicine at the University of Pennsylvania and a senior fellow at Penn's Center for Bioethics. "The 23andMe case is another example of the challenge between deciding when information ends and medical knowledge begins," Karlawish notes. "23andMe is full of information about your genetic code. Some of it is medical knowledge, and some of it is not. It's the medical knowledge that I don't think is being appropriately presented to people."

Karlawish adds that he is particularly concerned about how 23andMe handles the APOE genotype, which is associated with Alzheimer's disease. Studies have shown that people who carry one or two copies of a particular variant of the gene are at an increased risk of developing the disease, but the revelation that one's genotype contains that variation is minimally useful, at best: The direct correlation between the gene and the disease has yet to be fully understood, Karlawish says, and as of yet, there are no good therapies to treat or prevent Alzheimer's, anyway. "Anecdotally, we heard about a number of individuals who didn't know what they were walking into and suddenly learned their APOE result, much to their chagrin," he notes. "23andMe sent a lot of people on a wild goose chase trying to figure out what this all really means."

According to Karlawish, APOE testing is being used more practically in a study recently funded by the federal government, in which people with two copies of the APOE gene believed to increase their risk for Alzheimer's will be given a drug that purports to slow the rate of cognitive decline. "In that sense, there's a very useful role for APOE testing, which is to link it to enrollment in [drug] trials. That's when it's appropriate to do APOE testing in someone who's asymptomatic."

Staunch supporters of freedom of information might argue that everyone has the right to know what their genetic code says about them. While that may be true, it's important to remember that only a handful of diseases have been definitively linked to specific genes, says Robert Klitzman, a professor of clinical psychiatry at the Columbia University College of Physicians and Surgeons, and author of the book, *Am I My Genes? Confronting Fate and Family Secrets in the Age of Genetic Testing.*

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"We know that people don't understand genetics well, [and] they don't understand statistics well," Klitzman notes. "Physicians also don't know much about genetic testing. The question is: Can [direct-to-consumer genetic tests] cause distress? Yes. Can they cause people to get depressed and anxious? Yes. Will that be everyone? We don't know."

Recently, some medical organizations have been contemplating the best course of action to take when a well-known genetic link to a particular disease is found by accident — in patients who have their genomes sequenced for another purpose. Whole-genome sequencing is becoming more common, for example, among cancer patients whose oncologists want to use the information to find therapies that have worked well in similar patients, Klitzman points out. The American College of Medical Genetics and Genomics recently advised that those patients be told if they have genes that are associated with 24 treatable genetic conditions, including hereditary breast cancer, Marfan Syndrome and dilated cardiomyopathy. "The reason this is important is that some of these diseases are serious and actionable," meaning there are concrete actions patients can take to prevent or treat them, Klitzman says.

No Chill on Innovation

The interaction between the FDA and 23andMe provides important lessons for future health care entrepreneurs, according to Steven Nichtberger, a life sciences entrepreneur and adjunct professor at Wharton who manages the school's Life Sciences & Management capstone course on health care company formation, financing and leadership. "My impression of this situation from the warning letter is that the FDA bent over backwards to provide plenty of guidance, but it seems like 23andMe failed to be responsive to it and dropped the ball," Nichtberger says.

Indeed, the warning letter indicates that 23andMe submitted applications to the FDA for marketing approval on several occasions, but those documents "failed to address the issues described during previous interactions with the Agency."

Students in Nichtberger's capstone course, who are earning dual bachelor's degrees in economics and science, form management teams around novel medical advances — typically from Penn's medical school — and come up with strategies for bringing them to market. Mastering the regulatory system is "completely essential and a core piece of the class," Nichtberger notes. "We teach them to develop regulatory strategies so they do not go astray of the FDA."

According to Nichtberger, there's always a risk that FDA interference with high-profile companies like 23andMe could turn off other entrepreneurs in genetics, but he doesn't believe that should be the case. "It's my impression that in the last few years, the FDA and global regulatory authorities have begun to take a more patient-centric view of novel innovations, which allows them to begin to consider the risk/benefit profile of new products through the eyes of patients who need them. That allows them to apply different standards to different technologies. In order to implement that new approach, the FDA [has] made [itself] available for frequent and early interactions — especially with small companies — where complex technologies are at play."

To succeed, tomorrow's health care entrepreneurs will need to form close relationships with the FDA and other regulatory agencies from the get-go. Says Nichtberger: "If you have a novel product where the pathway is unclear, meet with the FDA early and often to identify a pathway that's agreeable to both you and FDA. That's how you mitigate the risk for you and your investors."