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Center for Devices and Radiological Health,
Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993-0002

**FDA Public Meeting
“Direct-to-Consumer Genetic Testing”
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INTRODUCTION

The Council for Responsible Genetics is a public policy organization that represents the public interest and fosters public debate about the social, ethical and environmental implications of genetic technologies. We appreciate the opportunity to comment on direct-to consumer genetic testing, our concerns regarding consumer protection and the need for responsible regulation.

COMMENTS

The Human Genome Project is properly regarded as one of the great scientific achievements of this generation. Since then, new technologies have emerged that are equally significant, reducing the cost of whole genome sequencing to a small fraction of its original cost and continuing to make impressive strides towards introducing genomics to the broader public through clinical applications of this technology.

As the science progresses, it has become clear that the major challenge for the future won't be sequencing technologies and broad public access to them but rather the cost and difficulty of interpreting and applying the huge amounts of data they generate.

We are still only at the beginning of the “genetic revolution” and it is certainly our hope that this new synthesis of genetics and information technology can empower individual self-knowledge and promote health across a wide variety of platforms. Yet, how medical care will be ultimately “personalized” is still unclear; as physicians move slowly to embrace genetic testing prior to the robust development of scientific knowledge and understanding over the relationships between genes, human health and the environment, private firms have scrambled to fill this void by offering these testing services direct-to-consumer (DTC).

These companies offer individuals the opportunity to discover if their genomes possess SNPs, and in some cases known Mendelian variants associated with disease and cancer risk, nutrient metabolism, drug response and metabolism, and recessive carrier states among others. They further offer risk assessment services, which look at several genes simultaneously to give probabilities of disease development over one’s lifetime, and offer diet and lifestyle recommendations on the basis of these genetic test results.

It is difficult to speak about the current state of the industry as whole, since there are some companies (such as 23andMe and Navigenics) that use high-quality genetic testing and who seek to leverage published and peer-reviewed scientific evidence and many other DTC genetics companies that are essentially fraudulent in their laboratory testing or claims.

However, there are significant concerns that we have for the industry as a whole, as it currently operates without regulation. Let me be clear, the call for regulation of DTC genetic testing is not some paternalistic denial of individual access to one’s own genome, nor some blind adherence to medical tradition. We believe everyone should have access to their genome and be able to sequence it if they choose. What we do feel strongly about, however, is that people shouldn’t be misled about the significance of that information and that people should be able to be assured that the claims that are made are accurate and that their privacy will be protected. We must acknowledge that information can cause both direct and indirect harms as well as good.

The value of DTC genetic testing to most consumers, the reason why most consumers would pay these private companies to sequence their genome is not for the sequencing itself, but for the perceived benefit of learning what such sequencing means for their health and that of their family. Science itself is incremental, and what we’ve learned through example after example over decades is that when dealing directly with human health, the integration of science with medicine and other consumer applications must be careful and methodical.

What does a set of genetic test results actually reveal? How will they actually improve clinical care and quality of life? We’re still very much in the process of learning the answers to these questions.

The marketing of genetic tests to consumers is following a path similar to direct-to-consumer marketing of prescription drugs. But unlike prescription drugs, genetic tests do not have to be federally approved or validated, and some of these tests may or may not do what the companies claim they can do. Furthermore, genetic tests are often patented. There are rarely second opinions or the possibility of retests by another company. Consumers have no recourse.

Reputable DTC companies may very well be doing a decent job of reliably telling the consumer which nucleotide they have at a given position. These companies are in a difficult position, though, they attempt to market their services while at the same time communicating the current limitations of what we can learn from genetic information. This may be one of the reasons they regularly caution that what they are offering isn't medical advice. Yet it is easy to overstate the significance of genetic results, particularly those tests for which reliability has not been certified and standardization has not been set by a professional genetics association.

And these companies want to have it both ways. They know full well that few consumers will purchase their products unless they can directly see the benefit of that information. And so these companies regularly make and market suggestive statements to the public. 23andMe's website states "Take Charge of Your Health and Wellness...Let Your DNA Help You Plan for the Important Things in Life." Navigenics website offers "A New Look for a Healthier Future" deCode Genetics promises to "decode Your Health" and Pathway Genomics claims that "It's Now Possible to Know How Genes May Affect Your Health." Every player in the industry makes both explicit and implicit claims that knowing your genetic information will demonstrably improve your health; with a few exceptions science is still progressing towards being able to make that case.

As the recent investigation of the DTC industry by the General Accounting Office clearly demonstrated, there's just no way of reconciling industry claims that the information they are providing is ready for provision directly to the consumer with the fact that reputable companies conduct analyses on the same DNA and come up with radically different interpretations. Indeed as research develops we are learning that genetics is only one small part of our risk for most of the diseases and conditions that these companies test for because the causation of these maladies is multifactorial.

The reason offered as to why DTC companies come up with different results is simply that different companies are testing a different set of variants. The solution offered, then, is that an agreed upon set of common standards would solve this problem. But this is only partially correct. The reason why this is not a complete solution is that we are still learning how to aggregate independent risk factors into a net risk score. Genes interact with each other and the environment in ways that we are only just beginning to understand. Even if there was agreed upon standards, and all these companies came up with the same risk prediction as a result, we just simply don't know enough at this point to know whether in most cases that prediction is a correct one.

A small percentage of the information that DTC companies offer, like BRCA1 and 2 (relating to risk of breast and ovarian cancer) are very predictive as these disorders are more fully penetrant, and in the right circumstances have important medical implications for a small number of people. In most cases, though, the magnitudes of the risk shift that DTC companies are giving people has limited value. Finding out that your risks are slightly increased or decreased over the general population is essentially meaningless since these are common diseases that we remain at significant absolute risk for whether or not we are at some relatively increased or decreased genetic risk. Moreover this risk information is delivered without reference to family history or lifestyle which makes it even less reliable as a risk indicator. Now some have argued by analogy that cholesterol and blood pressure are regularly tested for and they confer only subtle relative

risks for heart disease and this is similar to the degree of risk conferred by genetic variants. And that is true. But what they fail to mention is that your doctor doesn't check your cholesterol because they are primarily seeking predictive information. Your doctor checks your cholesterol because they can change your cholesterol. That is the actual value of such testing. By contrast, offering information about something such as diabetes risk by genotyping without reference to information about family history, weight or blood glucose is both misleading and harmful to the consumer.

The potential for harm to the consumer rises significantly when these companies combine clinically meaningful rare DNA variant information along with clinically much less relevant common DNA variant information and further pair such information with pure entertainment such as, for example, genetic tests for whether you have thick earwax. Do customers of DTC genetic testing services really understand what they are purchasing? Do they understand the results? Are the results accurate? Do they consult their physicians about the information? Are unnecessary medical tests ordered? At the present time, we simply do not have all the answers. Preliminary studies have had severe limitations in terms of representative populations. As the industry grows to serve larger and larger proportions of the general public, it is the duty of the FDA to ensure that the public is protected.

We have fallen demonstrably behind our colleagues across Europe in defining the limitations of DTC testing. The European Society of Human Genetics has called for an end to the overhyping of genetic tests, more and better evaluations of such tests, and more diligent regulation of these tests. Legislation covering genetic tests has been introduced at the national level in some European countries and eleven professional genetics societies in France have gone further by issuing a statement criticizing the underlying theoretical basis for calculating risk of common diseases based on multiple genetic variants and concluding: "While genome wide studies provide an essential contribution to scientific knowledge of multifactorial diseases, the isolated use of information provided by them lacks any capacity to predict future onset of those diseases. It leads to an erroneous perception of the risk for the individual."

We can and must do better to regulate direct-to-consumer genetic testing in our own backyard. CRG strongly believes DTC testing should be regulated under the Federal Food Drug and Cosmetic Act 21 U.S.C. 321(h), and therefore be subject to premarket approval requirements. We recommend the following steps be undertaken. Some, but not all DTC companies voluntarily engage in some of these practices to varying degrees. We believe they should be mandatory.

Oversight of test accuracy

We must insist on the provision of accurate and transparent information to consumers. We must not only require that CLIA-certified laboratories be used but also acknowledge the limitations of CLIA certification and require more rigorous standards for analytic validity. Specifically, DTC firms should disclose as part of premarket review data demonstrating a high level of analytical validity for all tests.

Oversight of clinical validity

a. DTC firms make broad claims about the association of certain SNPs and real human phenotypes, ranging from single-gene diseases such as cystic fibrosis to far more complicated and poorly understood multi-factor diseases such as diabetes. While some of the associations between genes and health conditions are grounded in rigorous scientific literature, many may not be. CRG believes that premarket disclosure of the relevant research demonstrating the validity of health claims on the basis of genotyping results should be required. This should include the sensitivity, specificity and predictive value of the test, as well as the populations for which it has been studied. Furthermore, direct-to-consumer medical tests must be honestly labeled as medical or nonmedical and be logically consistent. Such tests must be further defined by whether they have demonstrated utility, and such utility must be explained to the consumer.

b. DTC firms also interpret test results to give estimated numerical probabilities of disease risk, rather than narrower claims of positive or negative association. CRG encourages FDA to require DTC firms to disclose evidence regarding the accuracy and scientific validity of the methodology used in making these interpretations.

c. DTC companies also make health and lifestyle recommendations on the basis of the genetic risks they find. An analysis of these recommendations for scientific validity and clinical efficacy should also be disclosed to the FDA in premarket filings.

d. DTC genetic tests as well as the methodology used to interpret them and provide risk assessments satisfy the requirements for “medical devices” under 21 U.S.C. §360c(a)(1)(C). While some may argue that the interpretation of genetic tests in the form of risk assessments are analogous to interpreting MRI scans, for example, the lack of individualized interpretation significantly distinguishes these two practices. Another distinction is the lack of adequate counseling to assist consumers and patients in interpreting and acting on results. While genetic counselors may be available, consulting them is not mandatory for consumers, leaving open the risk that consumers may undertake risky decisions in response to results they do not fully understand.

Disclosure of possible risks

The potential risks of inaccurate test accuracy or invalid result interpretation can be great. Individuals can take drastic prophylactic measures in response to information about cancer risk, for example. Similarly, individuals could be persuaded by their results to forego necessary screening in response to information about a lack of risk. Furthermore, information regarding a genetic disposition for certain rates of drug metabolism or drug response can have a great effect on decisions about what therapies to pursue to treat current conditions. CRG believes that DTC firms must clearly and understandably disclose any risks associated with making decisions on the basis of genetic test results.

Furthermore, we are very concerned that after a year of Federal regulatory review of the DTC genetic testing industry that the Federal Trade Commission (FTC) has still not taken a visible role in such review. We urge the FDA to bring the FTC into this process to ensure that the consumer is protected from inaccurate and untruthful marketing.

PRIVACY

Finally, we are equally concerned that the many significant and unique consumer privacy issues implicated by direct-to-consumer genetic testing are not being addressed by these inquiries.

DNA provides a rich digital source of medical information; as a result it has great scientific value. But it is also ripe for data sharing and has significant commercial value as well. Purchasing genetic testing services in an online commercial marketplace raises significant privacy concerns, as consumers may turn over their DNA and other personally identifiable information to companies without a clear understanding of the privacy risks and without clear guidance as to their legal and regulatory rights in this area. While the FDA may not have full oversight over all these issues, we believe these issues must be fully aired in any discussion of the direct-to-consumer genetic testing industry and that the FDA , FTC and other agencies work together to comprehensively address those privacy issues within their purview.

There are currently no clear guidelines on the ownership of genetic material and the information derived from it, nor are there clear guidelines with respect to protection of customer privacy by the direct-to-consumer genetic testing industry. Indeed, consent forms and privacy policies vary widely within the industry and without standards can be unclear and often subject to change.

There are three specific areas where significant privacy concerns arise.

1) Controls on DNA Submitted by Customers

Current practices related to ensuring that customers are submitting only their own DNA are insufficient. At present, commercial personal genomics companies do require customers to confirm they have legal authority to submit DNA samples, yet such statements are not clearly and conspicuously posted but rather often hidden within larger privacy and consent documents which are often visible to the consumer only after the registration process has begun. Moreover, they do not explicitly warn customers of the possible issues raised by submitting another individual's DNA for analysis. Considering how simple surreptitious collection of individual DNA can be, it is not hard to imagine how political, social and personal motivations could compel the improper submission of DNA samples. This is a particular concern since most of these companies allow for an individual to purchase multiple testing kits per order. Yet, few controls are offered beyond such statements to ensure that customers are actually complying with this requirement. No offer of proof is requested beyond the statement. This could easily be included as part of the sample submission process.

2) Security of Genetic Information

Customers not only provide a DNA sample as part of their participation in the personal genomics marketplace. They are also offered a variety of surveys, blogs and other tools where they can provide personally identifiable information. Whenever identifiable DNA samples are collected and stored, there is a high risk that violations of genetic privacy will follow. The methodology by which this information is secured is essential, yet without standards and oversight we still

know very little beyond the assurances of the industry as to what specific controls are used. Moreover, the privacy policies of DTC companies are not subject to the health privacy regulations issued pursuant to the Health Insurance Portability and Accountability Act (HIPAA) and there few state and federal privacy laws that apply. It is essential that personal information should be protected by security safeguards appropriate to the sensitivity of the information. Safeguards should include physical, technical and administrative measures to protect information and biological samples from unauthorized access, use, disclosure, alteration or destruction.

Almost all the DTC company privacy policies make statements about security safeguards, though the degree of detail varies substantially. There is also no transparency as to the degree to which personally identifiable health information is de-identified. As the ability to share, store, and aggregate genomic data progresses, the capability of keeping this data anonymous becomes increasingly important. Because an individual's genetic information is so personal and specific, it is vital to protect it from any unwarranted access or use. There have been several instances where de-identified data has been re-identified and personal information linked back to its owner. One such study¹ achieved reidentification of DNA data and established identifiable linkages in 33-100% of surveyed cases, which focused on eight gene based diseases. The professors used anonymized DNA database entries, and related the information to publicly available health information despite the fact that the database did not include any explicit identifiers, such as name, address, social security number, or any other personal information. Because not all de-identification techniques adequately anonymize data, it is important that the process employed by the industry is robust, scalable, transparent and shown to provably prevent the identification of customer information.

3) Third Party Disclosure of Customer Data

One significant unresolved issue relating to the DTC industry is exactly who owns the customer's data. Most DTC companies do not explicitly address this issue in their privacy policies. If the DNA sample and other information submitted by the customer are the property of the company, the company is free to sell or otherwise transfer that information to a third party.

Many DTC companies have adopted this approach as part of their business model without sufficiently explaining to customers the extent to which this may occur and the potential negative consequences. Moreover how such information is to be treated upon sale of a company or if a company enters bankruptcy proceedings, particularly when the entities potentially acquiring such information have significantly less strict privacy standards, is less than clear and is certainly not expressed to customers.

Most DTC companies do not ask for specific consent for these purposes. Some companies are moving in the right direction. 23andMe has begun asking for specific consent for participation in published research. However, they note that even by refusing to participate, "we may still use your Genetic and/or Self-Reported Information for R&D purposes as described above, which may include disclosure of Aggregated Genetic and Self-Reported Information to third-party non-profit and/or commercial research partners who will not publish that information

¹ Bradley Malin and Latanya Sweeney, Determining the Identifiability of DNA Database Entries, 2001 Journal of the American Medical Informatics Association 423.

in a peer-reviewed scientific journal.”² The degree to which these types of partnerships and others have proliferated within the industry is still largely unclear. What is clear is that it is essential that affirmative written consent must be required before DTC companies can use any customer generated genetic information in this way.

There is currently very little guidance on how consumers can protect their privacy. For example, the US Federal Trade Commission gives the following advice to consumers who are considering DTC genetic tests: “Protect your privacy. At-home test companies may post patient test results online. If the website is not secure, your information may be seen by others. Before you do business with any company online, check the privacy policy to see how they may use your personal information, and whether they share customer information with marketers.”³ Such advisories are hardly satisfactory to ensure consumer privacy is protected.

We urge the FDA and other Federal agencies to open separate inquiries into these vital consumer protection issues.

CONCLUSION

We ask that the Food and Drug Administration, in concert with other Federal agencies, work together to help set industry standards and strong public oversight for responsible and accountable practices in the direct-to-consumer genetic testing industry and ensure all issues regarding industry practice are adequately supervised. The Council for Responsible Genetics is glad to offer any assistance it can provide as this process continues to unfold.

² 23andme Privacy Statement (accessed on 2/22/11 at <https://www.23andme.com/about/privacy/>)

³ See, for example, United States, Federal Trade Commission, *At-home Genetic Tests: A Healthy Dose of Skepticism may be the Best Prescription* (2006), (accessed on 2/22/11 at <http://www.ftc.gov/bcp/edu/pubs/consumer/health/hea02.shtm>.)