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FDA public meeting on Oversight of Laboratory Developed Tests

“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 current concerns with the industry and our firm belief that responsible oversight of the industry is necessary.

COMMENTS

While genetic testing has grown as a medical practice over the past decade, the range of gene variations tested for clinically remains narrow. This is due to many reasons, including the cost of testing and physicians' ability to rely on other indicia of disease risk, including family history and physiological measurements. Primarily, however, physicians have been reluctant to delve into genetic testing prior to the robust development of scientific knowledge and understanding over the relationships between genes, human health, human environment and lifestyle.

Despite such reluctance on the part of healthcare providers to order and interpret genetic tests, private firms have scrambled to offer these testing services direct-to-consumer (DTC). These companies offer individuals the opportunity to discover if their genomes possess SNPs

associated with disease and cancer risk, nutrient metabolism, and drug response and metabolism, 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.

Many of these associations and interpretations, however, are based on incomplete, inconclusive scientific evidence from which DTC companies extrapolate exaggerated conclusions. Furthermore, the scientific basis for test result interpretations and risk calculations remain trade secrets and are therefore not disclosed to consumers. Beyond such questions regarding the clinical validity of DTC genetic tests, the analytical validity - the accuracy of the genetic tests for SNP variations - is also largely unknown to consumers and regulators.

Nevertheless, the risk posed to consumers by faulty information remains very high. Consumers may make drastic prophylactic medical procedures when faced with high cancer risk, for example, or dismiss important preventative and screening recommendations in light of information they are at a low genetic risk. Where the link between genetics and risk is dubious, these decisions may be medically dangerous. Furthermore, consumers may rely on information regarding drug tolerance and metabolism in deciding how to medicate existing diseases - important medical decisions that should be made on the basis of scientifically sound assumptions. Finally, the information provided to consumers - both regarding genetic risk and information regarding familial genetic relationships - can have significant psychological and emotional impacts.

For these reasons, the Council for Responsible Genetics urges the FDA to expand its current regulatory regime to encapsulate DTC genetic testing. Specifically, CRG recommends that premarket submissions be required disclosing the clinical and analytical validity of genetic tests, genetic test result interpretation methodologies, and any risks associated with consumers' reliance on such tests.

1. Oversight of test accuracy

- a. DTC tests currently provide genotyping analysis. These tests scan the genome for matches to previously identified SNPs which are putatively associated with human phenotypes - ranging from disease risk to physical appearance. While the laboratories performing these tests must be CLIA-certified, and must therefore meet certain quality-control criteria, we believe greater oversight from the FDA is necessary. Specifically, DTC firms should disclose as part of premarket review data demonstrating a high level of analytical validity for all tests.

2. 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.

- 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 genetic testing companies 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.

3. Disclosure of possible risks

- a. The potential risks of inaccurate test accuracy or valid result interpretation can be great. Patients can take drastic prophylactic measures in response to information about cancer risk, for example. Similarly, patients may 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.
- b. There have been few studies documenting potential psychological risks associated with genetic test results. The lack of studies, however, does not eliminate the real possibility that knowing one has a high risk of dangerous or deadly disease can be highly damaging. These risks should be evaluated when weighing the risks and benefits of potentially faulty or scientifically unsound test results.
- c. Genetic information is also highly relevant to family relationships. Both accurate and faulty data can bring these relationships into question, for example, by revealing false paternity. The risk of discovery such information should also be disclosed to consumers, as well as the risk of any potential psychological effects that result.

CRG strongly believes DTC testing should be regulated under Federal Food Drug and Cosmetic Act 21 U.S.C. 321(h), and therefore be subject to premarket approval requirements. Specifically,

we urge the FDA to request that data demonstrating the clinical and analytical validity of all genetic tests and analytical tools – including algorithms or software programs that calculate disease risk based on several SNPs – be submitted to ensure accuracy and validity. CRG also urges the FDA to require disclosures regarding the scientific evidence behind health and lifestyle recommendations given to consumers on the basis of genetic test results. Furthermore, we believe DTC firms should be mandated to disclose the accuracy, sensitivity and predictability of any results to consumers and patients. Finally, we encourage the FDA to require that DTC companies disclose potential psychological, personal and health risks associated with both inaccurate results and uncertain clinical validity.

ADDITIONAL PRIVACY CONCERNS:

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. Mistakes and other breaches of security are not uncommon. Just last month, the DTC company 23andMe accidentally sent data of up to 96 individuals to the wrong customers.

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 re-identification 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.

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

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. For example 23andMe has partnerships with the Swiss firm Mondobiotec and the Parkinson's Institute and Navigenics is conducting studies with the Mayo Clinic and Scripps Institute. 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 recently 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...which may include disclosure...to third-party non-profit and/or commercial research partners who will not publish that information 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.

CONCLUSION:

We strongly encourage the Food and Drug Administration, as well as the Federal Trade Commission, and the Centers for Disease Control to 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 7/12/10 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), online: Federal Trade Commission <http://www.ftc.gov/bcp/edu/pubs/consumer/health/hea02.shtm>.