

PATHWAY GENOMICS

RESPONSE TO REPORT RELEASED BY UNITED STATES GOVERNMENT ACCOUNTABILITY OFFICE

DIRECT-TO-CONSUMER GENETIC TESTS Misleading Test Results Are Further Complicated by Deceptive Marketing and Other Questionable Practices Released July 22, 2010, 9:30am EDT

On July 22, 2010, simultaneous with the hearing on “Direct-To-Consumer Genetic Testing and the Consequences to the Public Health,” held by the Subcommittee on Oversight and Investigation of the U.S. House of Representatives’ Committee on Energy and Commerce, the U.S. Government Accountability Office (GAO) released its report titled, “Direct-To-Consumer Genetic Tests: Misleading Test Results Are Further Complicated by Deceptive Marketing and Other Questionable Practices.” This report, coupled with the testimony of Gregory Kutz, Managing Director of Forensic Audits and Special Investigations for GAO, unfairly portrayed Pathway Genomics as providing genetic reports directly to consumers in a manner that GAO considered inaccurate and irresponsible.

While we acknowledge that the Congressional hearing and the GAO report did highlight areas of legitimate concern to the entire genetic testing industry, this document seeks to correct the record on several serious flaws and inaccuracies in the GAO report and testimony.

Pathway Genomics is not a “Direct-to-Consumer” Genetic Testing Company

Consumer genetic testing companies that allow customers to order and receive test results without the involvement of a licensed physician are known in the industry as direct-to-consumer (DTC) companies. Although described as a DTC genetic testing company, it is important to understand that Pathway Genomics is not a DTC company. Nevertheless, as part of our ongoing dialogue with FDA, we recently suspended the ability to order our genetic reports directly from our website.

Pathway Genomics has always required and provided expert physician and genetic counselor review and oversight of our genetic testing services. All reports are reviewed by an expert physician prior to delivery, and customers are provided free access to genetic counselors and on-staff medical doctors to help them understand what their test results mean, and what they do not mean. Furthermore, Pathway chose to follow the 2008 recommendation of the Federal Trade Commission that “all genetic tests be done in a specialized laboratory and that a doctor or counselor with specialized training interpret the results” to provide consumers with accurate and safe testing services.

GAO's report provided only a limited and partial picture of genetic testing

In its report, GAO emphasizes that they “did not conduct a rigorous scientific study” of the data it gathered. Yet GAO’s report and testimony make many unequivocal statements and claims about the inaccuracy and limited utility of genetic testing and reporting as if they are based on scientific fact.

GAO identified differences between the companies only in their reporting of complex health conditions, and made no mention of the other two sections of our report, which pertain to the carrier status of recessive genetic conditions and the genetics of drug (medication) response. Failure to discuss these other areas, and selectively focusing on areas of perceived differences, misrepresents the uniformity and scientific rigor applied to these services. In fact, one witness at the hearing, Dr. Evans, admitted, “some of the information in these genetic scans has robust genetic and medical implications,” and he went on to say he would use this information in his practice.

The GAO report and testimony focused on areas where there were discrepancies in risk of health conditions between the companies, but a comprehensive analysis shows a general pattern of consistency across the reporting companies. Of 133 conditions presented in the GAO report that were analyzed by more than one company, the majority if not all companies were in complete agreement about the relative risk of that disease in 103 cases, more than 77% of the time. The reporting companies were in complete disagreement in only 10 cases, or just 7.5% of cases reported by GAO (Figure 1).

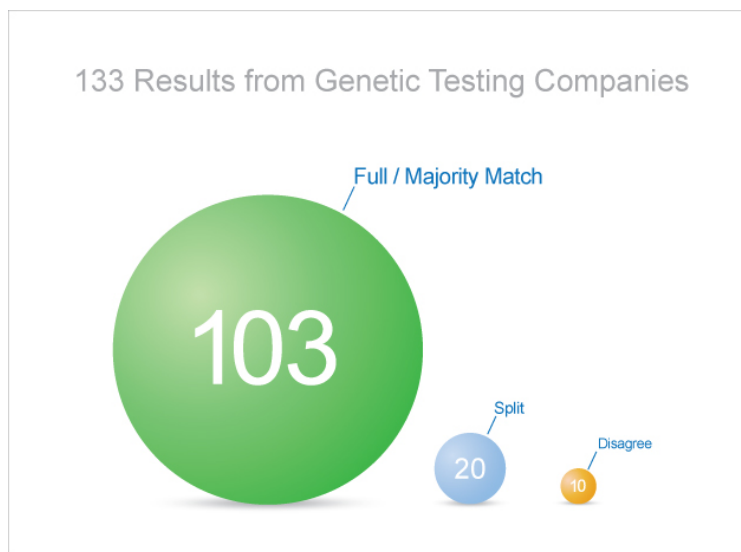


Figure 1.

The recommendations of the committee to establish some common standards for reporting genetic risk estimations will help to further reduce the observed differences, but the conclusion that "[d]ifferent companies often provide different results" overstates the results based on a minority of the cases. It is widely accepted that the underlying genotype data is highly accurate yet there may be different interpretations produced by different algorithms. This is a common occurrence in health care, as there are several scientifically valid risk calculators that will produce different levels of risk for the same patient. For example, the Entelos and Archimedes models are used to estimate diabetes risk, and the Reynolds Risk Score and the National Cholesterol Education Program are used for predicting the risk for cardiovascular disease. Just as different practitioners can offer varying opinions on medical diagnosis and treatment, differences in risk estimation should not be construed as undermining the validity of genetic testing.

GAO's finding that risk predictions sometimes conflict with medical history does not undermine validity of genetic testing

GAO misleadingly reported on alleged discrepancies between genetic testing and family or medical histories for select conditions. However, the GAO report only provides part of the story.

The GAO report highlights discrepancies in family history of heart disease, and genetic risk for heart attack for Donor 2. The genetic reports classified Donor 2 with an average genetic risk for heart attack. However, heart disease is a much broader condition that includes heart attack, atrial fibrillation, coronary artery disease, and other cardiovascular diseases. It should be noted that all three companies called to testify agreed that Donor 2's factual profile had an increased genetic risk for atrial fibrillation.

The GAO report also highlighted Donor 4, who had a pacemaker implanted to treat atrial fibrillation, but his genetic risk for atrial fibrillation ranged from below average to average. As we emphasized in our testimony, and as we make clear in our customers' reports, genetic risks are only one part of the risk contributing to the development of a disease or condition. It is widely accepted that the risk of developing a condition depends not only on genetic factors, but also environmental and lifestyle factors. Pathway Genomics asks customers to complete a health, lifestyle and family history questionnaire so that we can report genetic risk in context of lifestyle choices. There are many examples in our database for which people with a self-reported family history of a complex disease have average genetic risk and very high lifestyle risk for that condition. Therefore, the fact that a single person may have average or below average risk of developing a condition, but actually does develop that condition, is not inconsistent with genetic testing.

Donor 4 (discussed immediately above) was a colon cancer survivor, and the testimony failed to highlight that all three testifying companies identified him as having an increased risk. Similarly, for Donor 5, who has a family history of Alzheimer's disease, all of the companies testing for that condition show high genetic risk for Alzheimer's disease for this

person (23andme does not report Alzheimer's disease risk). It is disappointing that the GAO testimony did not choose to highlight these results.

The GAO analyses represent a fundamental misunderstanding of the information provided by genetic testing for complex health conditions. Pathway Genomics uses a combination of the latest scientifically validated and published genetic research, a person's health history, family health history, environmental factors, as well as his or her genetic profile to help them understand if people with similar genetics have a higher or lower incidence of disease.

It is important to note that these risk estimations are a relative measure of risk as compared to the general population and not a prediction or diagnosis of disease. Risk factors alone do not predict the occurrence of disease, but are used to help individuals, clinicians, and policy makers make informed decisions about managing and preventing disease. Genetic risk information on complex health conditions is no different.

For example, it is well accepted that smoking increases one's risk of lung cancer. That does not mean, however, that all smokers will develop lung cancer. In fact, only 17.2% of male smokers develop lung cancer and just 11.6% of female smokers develop lung cancer.¹ The fact that nearly 9 in 10 female smokers do not develop lung cancer does not discredit the fact that they are at higher risk, nor should the presentation of a non-smoking individual with lung cancer challenge the scientific conclusion that smoking increases risk and people should be encouraged not to smoke. Yet, such conclusions are exactly what GAO made in its assessment of genetic testing companies.

GAO's criticisms of differences in reports for different ethnic groups are without merit

In this section of the report, GAO states, "most genetic research has only been done on persons of European ancestry and therefore such individuals receive more accurate results." We are not able speak for the other companies, but it is exactly for this reason that Pathway Genomics' reports for non-Caucasians do not receive the same number of test results as do Caucasians. The GAO report is correct, as the majority of research published to date has been accomplished using Caucasian populations of European ancestry; therefore, the quality of scientific research limits the amount of information that we can accurately provide to African, Hispanic or Asian individuals.

We do not know when GAO analyzed our website, but well before the hearing we provided a clear table demonstrating the information that is available to individuals of different ethnicities as shown in Figure 2 of the Appendix. This chart is also available on our website at the following URL: <http://www.pathway.com/dna-reports/full-list-of-conditions>.

The GAO report characterized this disparity as both inaccurate and deceptive when, in fact,

¹ Villeneuve, PJ; Mao Y (November 1994). "Lifetime probability of developing lung cancer, by smoking status, Canada." *Canadian Journal of Public Health* 85 (6): 385-388.

Pathway's approach is the result of a conscientious effort to be accurate based on the current state of scientific research. As additional research on these ethnicities becomes published, we update our services to incorporate the additional information and have provided the updated reports at no additional charge.

Secretly taped telephone conversation between GAO investigators and Pathway Genomics

GAO investigators secretly recorded a telephone conversation with a Pathway customer service representative, during which the GAO agent inquired about surprising her fiancé with a DNA report.

Our customer service representative understood the caller to be asking if she could *purchase a DNA collection kit* for her fiancé to submit for testing, *not* for surreptitiously *acquiring* a saliva sample from him and submitting it for testing without his consent, as portrayed by GAO.

Immediately after this phone conversation concluded, the conversation was brought to the attention of Pathway's management team. To ensure that there was no gray area in the understanding of our consent policies, our customer service agents received additional training to ensure that tests be approved only with proper consent.

It is important to note that the full context of this conversation is unknown as GAO chose not to release full transcripts or recordings of the conversations. It is also unknown how many positive calls and conversations were recorded between representatives of Pathway Genomics and the GAO investigators that initiated contact and purposefully misled our employees while misrepresenting their identities. Furthermore, it typically takes 5 to 15 minutes of conscious effort to provide enough saliva for our testing, and it is difficult to imagine that someone could collect this from a person without his or her knowledge.

GAO's testimony and report unfairly associated Pathway and the other testifying companies with improper marketing practices

We wholeheartedly agree with GAO's assessment that some of the companies in the report are engaging in practices that have no place within the scientific and medical community. Unfortunately, the companies engaging in the most egregious instances of this were not identified in the report and were not included in the hearing.

Consequently, the "bottom-feeder" genetic testing companies, representing the most flagrant marketing and business practices, remain anonymous. By selectively identifying Pathway Genomics, 23andme and Navigenics, GAO unfairly and inaccurately associated the three scientifically responsible companies with the questionable practices that were identified in GAO's report.

Pathway Genomics does not engage in deceptive marketing, misinformation, or questionable business practices, including the marketing or selling of nutritional

supplements or advising customers that supplements can cure diseases.

Expert physician involvement and oversight

The GAO report states that many doctors and healthcare practitioners cannot keep up with the pace of genetic tests and are not adequately prepared to use test information to treat patients appropriately, and therefore the tests have virtually no value.

This skewed logic is akin to blaming smart-phone developers for the inability of phone networks to provide adequate coverage and bandwidth. Since its inception, Pathway has made expert physicians and genetic counselors available, at no additional charge, to assist our customers and their physicians in understanding the information in their genetic reports.

Conclusion

We share the concerns of the United States Government Accountability Office that personalized genetic testing should be safe and useful for consumers. It is for this reason that Pathway Genomics completes all testing on-site at our CLIA-certified laboratory and that all tests are performed by trained genetic experts. Furthermore, to ensure customer safety, medical doctors and genetic counselors are made available to all customers before, during, and after testing to make sure qualified genetic specialists answer any questions.

As we presented above, we believe that GAO's report and testimony presented an incomplete and misleading picture of the scientific rigor and utility offered by Pathway specifically, and genetic testing generally.

We acknowledge that the GAO report has illuminated opportunities for improvement for both Pathway Genomics and other companies within the field of genetic testing. We also recognize the need to work closely with other responsible companies and FDA to ensure that high standards and good laboratory practices are implemented across the industry, to provide safe, reliable and useful genetic data to consumers who have a right to know this information.

Appendix

Condition	African	Asian	Caucasian	Hispanic
Age-related macular degeneration		✓	✓	
Alzheimer's disease, late onset	✓	✓	✓	✓
Amyotrophic lateral sclerosis (sporadic)			✓	
Asthma			✓	✓
Atrial fibrillation		✓	✓	
Breast cancer (females only)	✓	✓	✓	✓
Colorectal cancer		✓	✓	
Coronary artery disease		✓	✓	
Diabetes, Type 1		✓	✓	
Diabetes, Type 2	✓	✓	✓	
Exfoliation Glaucoma			✓	
Hypertension		✓	✓	
Leukemia, chronic lymphocytic			✓	
Lung cancer		✓	✓	
Melanoma			✓	
Multiple sclerosis			✓	
Myocardial infarction		✓	✓	
Obesity		✓	✓	
Osteoarthritis		✓	✓	
Parkinson's disease		✓		
Peripheral arterial disease			✓	
Prostate cancer (males only)	✓	✓	✓	✓
Psoriasis			✓	
Rheumatoid arthritis		✓	✓	
Systemic lupus erythematosus	✓	✓	✓	✓
Ulcerative colitis		✓	✓	

Figure 2: Health conditions reported by ethnicity