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AT HOME DNA TESTS: MARKETING SCAM OR MEDICAL BREAKTHROUGH

HEARING

BEFORE THE

SPECIAL COMMITTEE ON AGING
UNITED STATES SENATE

ONE HUNDRED NINTH CONGRESS

SECOND SESSION

WASHINGTON, DC

JULY 27, 2006

Serial No. 109–29

Printed for the use of the Special Committee on Aging

U.S. GOVERNMENT PRINTING OFFICE

30–711 PDF WASHINGTON : 2006

For sale by the Superintendent of Documents, U.S. Government Printing Office
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AT–HOME DNA TESTS: MARKETING SCAM OR MEDICAL BREAKTHROUGH?

THURSDAY, JULY 27, 2006

U.S. SENATE,
SPECIAL COMMITTEE ON AGING,
Washington, DC.

The Committee met, pursuant to notice, at 10:03 a.m., in room SD–106, Dirksen Senate Office Building, Hon. Gordon H. Smith (chairman of the committee) presiding.

Present: Senators Smith and Talent.

OPENING STATEMENT OF SENATOR GORDON H. SMITH, CHAIRMAN

The CHAIRMAN. Good morning, ladies and gentlemen. We welcome you to this hearing of the U.S. Senate Special Committee on Aging. This morning's topic is "At Home DNA Tests: Marketing Scam or Medical Breakthrough."

We will be exploring the regulatory and scientific issues relating to direct-to-consumer genetic tests. Genetic science holds great promise, and with that promise a hope for a better understanding of human health and disease. Recent advances in genetic science have fueled the growth of a direct-to-consumer genetic testing industry. With a few clicks on the Internet, consumers can now purchase at-home tests that claim to predict propensities for a myriad of health conditions, including Alzheimer's, cancer, diabetes and arthritis.

However, as reported just last month in the Washington Post, these home tests can shock and misinform consumers. The American College of Medical Genetics has advised the public to avoid home DNA tests, which it has called, quote, "potentially harmful," citing the possibility of inappropriate test utilization and misinterpretation of test results and a lack of follow-up.

Just today, the Federal Trade Commission, in conjunction with the Food and Drug Administration and the Centers for Disease Control, have released a consumer alert cautioning consumers that, quote, "Some of these tests lack scientific validity and others provide medical results that are meaningful only in the context of a full medical evaluation," end of quote.

These concerns give rise to questions about the oversight of the tests and the science behind them. The sales companies and testing laboratories currently operate apparently, unfortunately, in a regulatory abyss between jurisdictions of the FTC, the FDA and the CMS. Further, unclear direction from the agencies about their jurisdiction, a 6-year delay by the administration in promulgating a

genetics testing specialty rule under the Clinical Laboratory Improvement Amendments and regulatory loopholes have created an environment ripe for consumer fraud and abuse.

It is my concern about that environment that is ripe for consumer fraud and abuse which has necessitated this hearing today. This Committee has had a long history of trying to especially protect the senior citizens of this country against those who would perpetrate on them things which have less than value.

I have numerous questions regarding the marketing practices of the companies selling these tests to consumers, as well as the clinical practices of the laboratories performing the tests. I also have serious concerns about the tests' true predictive value and what is in many instances the lack of a health care professional's involvement to help consumers determine the necessity of testing and the meaning of the test results. I would like some level of assurance that the tests are safe, accurate and useful, and that there are basic privacy protections in place.

The expansion of genetic testing services also raises important ethical and legal questions about how these tests should be administered and what level of protection is necessary for sensitive medical and personal information provided by consumers when ordering these tests. It is my hope that through today's hearing, we will find answers to these questions.

This morning, we will hear from the Government Accountability Office about the results of their year-long investigation into the direct-to-consumer genetic testing industry. We also will hear from industry stakeholders and regulatory agencies charged with oversight of genetic testing. I am deeply disturbed by GAO's finding that consumers are being misled and exploited, and I am shocked to learn how little the Federal Government is doing to help consumers make informed decisions about the legitimacy of these tests.

Because of the nature of today's hearing, the Committee will be receiving all testimony under oath. I will administer the oath to each panel as a group and ask all of our witnesses to please be sworn in and to promise to tell the truth. After I administer the oath, I would ask that the panel witnesses each, in turn, one after another, individually acknowledge their affirmation to the oath by stating "I do." With that, I would ask the first panel of witnesses to stand and raise your right hands.

Do you promise to tell the truth, the whole truth, so help you God?

Mr. KUTZ. I do.

Dr. HUDSON. I do.

The CHAIRMAN. Our first panel includes Mr. Greg Kutz, who is the managing director of Forensic Audits and Special Investigations at the Government Accountability Office. Mr. Kutz and his team have spent the past year canvassing the direct-to-consumer genetic testing industry, purchasing test kits, obtaining test results, and consulting with experts and conducting site visits at the companies and laboratories involved in the industry. I commend Mr. Kutz and his team for their fine work, and we very much look forward to hearing your investigative results.

He will be followed by Kathy Hudson, who is the director of the Genetics and Public Policy Center at Johns Hopkins University. She will provide her expert opinion regarding various ethical, legal and social concerns relating to direct-to-consumer genetic testing.

I appreciate both of you being with us. Greg, why don't we start with you?

STATEMENT OF GREGORY KUTZ, MANAGING DIRECTOR, FORENSIC AUDITS AND SPECIAL INVESTIGATIONS, U.S. GOVERNMENT ACCOUNTABILITY OFFICE, WASHINGTON, DC

Mr. KUTZ. Mr. Chairman, thank you for the opportunity to discuss genetic testing. Our investigation relates specifically to certain genetic test kits sold directly to consumers on the Internet. The companies marketing these kits claim to provide consumers with lifestyle programs based on their genetically determined health risks. You asked us to investigate the legitimacy of these claims.

My testimony has two parts: first, how we conducted our investigation, and, second, our key findings. First, we investigated four websites selling what are referred to as nutrigenetic tests. These sites claimed that their tests would analyze between 4 and 19 genes, and provide personalized lifestyle recommendations. The cost of the kits that we purchased ranged from $89 to $395. We purchased several of the same kits from each website so that we would have a variety of results to analyze.

To test the legitimacy of these products, we created 14 fictitious consumers. As shown on the poster board, we used DNA from a female for 12 of these consumers and DNA from a male for 2 of the consumers. For all 14 kits, we submitted cheek swabs, 12 from a 9-month-old female and 2 from a 48-year-old male. In addition to the cheek swab, one company required us to submit a urine sample. We also sent in cheek swabs from a dog, a cat and several blanks, which were all returned to us because they could not be processed.

For each fictitious consumer, we filled out a questionnaire, pretending to be adult men and women of various ages, weights and different lifestyles. The questionnaires asked us about exercise, smoking, diet and vitamins taken, but did not ask us about any medical conditions we had or medications that we were taking. In assessing the results of the 14 fictitious consumers, we consulted with experts primarily in the areas of genetics and nutrition. We also interviewed representatives from the four websites and two labs processing the results.

Now that I have set up what we did, let me go on to my second point, our key findings. The poster board shows the medical conditions predicted for the 14 fictitious consumers based on the DNA that we submitted. As you can see, our consumers are at risk of developing osteoporosis, cancer, type 2 diabetes, heart disease and brain aging. Although all four websites said the kits were not intended to diagnose a disease, all 14 consumers were told they were at risk of developing these very serious medical conditions.

The primary problem here is that according to the experts, none of these predictions can be medically proven at this time. Research related to the genetic connection to the development of these conditions is at a very early stage, with many issues to be resolved.

The secondary problem is that the predictions use ambiguous language that renders them meaningless. For example, several results said the consumer may be at increased risk of developing heart disease. In other words, you might have an increased chance of developing heart disease. These predictions could apply to any human submitting DNA.

Websites 1 and 4 also recommended supplements, supposedly based on a consumer's unique DNA. However, our testing showed that these supplements are, in fact, not unique. For example, for website 1, two of our fictitious consumers were recommended the very same unique supplement. However, one of the consumers was actually the female and the other was actually the male.

Further, the next poster board shows that the supplement from website 1 contained the same ingredients, although in different amounts, as a multivitamin that we purchased at Rite-Aid. Look at the cost comparison: $1,200 per year for the supplement compared to $35 a year for the Rite-Aid multivitamin.

Although not identical, the expert nutritionists that we spoke to said that the costly supplement and the Rite-Aid vitamin would likely provide the same nutritional benefits for most people. Also, they expressed concern about the amount of vitamin A, B–6 and iron in the supplements that could be harmful.

Finally, the results from websites 1, 2 and 3 promise recommendations based on a consumer's unique genetic profile. However, our test shows that we could have created any lifestyle description and the results would simply echo the data submitted. For example, we submitted the same DNA for nine fictitious consumers and received advice that varied, clearly showing that the results are based on the questionnaire and not the DNA.

In conclusion, in a best-case scenario the test kits and supplements that we investigated provide little or no value to consumers. In a worst-case scenario, the test results could frighten a consumer into thinking that they will develop cancer, osteoporosis, heart disease, or brain aging. The fear could also cause them to purchase supplements at outrageous prices.

I understand that there is great potential for genetic testing and I don't want the results of our investigation to cast any shadows on the progress made to date. However, for the products that we tested, I want to send a message to consumers across the country: buyer beware. Before buying any of these products, consumers should not only think twice, but should consult with their doctor.

Mr. Chairman, this ends my statement. I look forward to your questions.

[The prepared statement of Mr. Kutz follows:]

United States Government Accountability Office

GAO

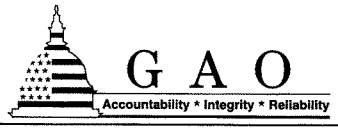
Testimony
Before the Special Committee on Aging, U.S. Senate

For Release on Delivery
Expected at 10:00 a.m. EST
Thursday, July 27, 2006

NUTRIGENETIC TESTING

Tests Purchased from Four Web Sites Mislead Consumers

Statement of Gregory Kutz, Managing Director
Forensic Audits and Special Investigations



GAO-06-977T

July 27, 2006

GAO
Accountability·Integrity·Reliability

Highlights

Highlights of GAO-06-977T, testimony before the Special Committee on Aging, U.S. Senate

NUTRIGENETIC TESTING

Tests Purchased from Four Web Sites Mislead Consumers

Why GAO Did This Study

Scientists increasingly believe that most, if not all, diseases have a genetic component. Consequently, genetic testing is becoming an integral part of health care with great potential for future test development and use. Some genetic tests are sold directly to the consumer via the Internet or retail stores, and purport to use genetic information to deliver personalized nutrition and lifestyle guidance. These tests require consumers to self-collect a sample of genetic material, usually from a cheek swab, and then forward the sample to a laboratory for analysis. Companies that market this type of test claim to provide consumers with the information needed to tailor their diet and exercise programs to address their genetically determined health risks.

GAO was asked to investigate the "legitimacy" of these claims. This testimony reflects the findings of GAO's investigation of a nonrepresentative selection of genetic tests. Specifically, GAO purchased tests from four Web sites and created "fictitious consumers" by submitting for analysis 12 DNA samples from a female and 2 samples from an unrelated male, and describing this DNA as coming from adults of various ages, weights, and lifestyle descriptions. GAO also consulted with experts in genetics and nutrition.

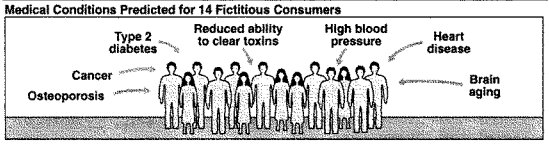
www.gao.gov/cgi-bin/getrpt?GAO-06-977T.

To view the full product, including the scope and methodology, click on the link above. For more information, contact Greg Kutz at 202-512-7455 or kutzg@gao.gov.

What GAO Found

The results from all the tests GAO purchased mislead consumers by making predictions that are medically unproven and so ambiguous that they do not provide meaningful information to consumers. Although there are numerous disclaimers indicating that the tests are not intended to diagnose disease, all 14 results predict that the fictitious consumers are at risk for developing a range of conditions, as shown in the figure below. However, although some types of diseases, such as cystic fibrosis, can be definitively diagnosed by looking at certain genes, the experts GAO spoke with said that the medical predictions in the tests results can not be medically proven at this time.

Medical Conditions Predicted for 14 Fictitious Consumers



Source: GAO.

Even if the predictions could be medically proven, the way the results are presented renders them meaningless. For example, many people "may" be "at increased risk" for developing heart disease, so such an ambiguous statement could relate to any human that submitted DNA.

Results from the tests that GAO purchased from Web sites 1 and 4 further mislead the consumer by recommending costly dietary supplements. The results from the tests from Web site 1 suggested "personalized" supplements costing approximately $1, 200 per year. However, after examining the list of ingredients, GAO found that they were substantially the same as typical vitamins and antioxidants that can be found in any grocery store for about $35 per year. Results from the tests from Web site 4 suggested expensive products that claimed to repair damaged DNA. However, the experts GAO spoke with stated that there is no "pill" currently available that has been proven to do so. The experts also told us that, in some circumstances, taking supplements such as those recommended may be harmful.

In addition, results from the tests that GAO purchased from Web sites 1, 2, and 3 do not provide recommendations based on a unique genetic profile as promised, but instead provide a number of common sense health recommendations. If the recommendations were truly based on genetic analysis, then the 9 fictitious consumers that GAO created for these sites using the female DNA should have received the same recommendations because their DNA came from the same source. Instead, they received a variety of different recommendations, depending on their fictitious lifestyles. For example, when GAO created lifestyle descriptions stating that the consumers smoked, they received recommendations to stop smoking. In contrast, if GAO said the consumers never smoked, they received recommendations to continue to avoid smoking.

Mr. Chairman and Members of the Committee:

Thank you for the opportunity to discuss our investigation of genetic tests that are sold directly to the consumer via the Internet, retail stores, or pharmacies. Recent advances in science have shown that the human genome is made up of about 20,000 to 25,000 genes, which are in turn made up of DNA.[1] These genes play a critical role in normal biological function, and scientists increasingly believe that most, if not all, diseases have a genetic component. Variants in these genes may increase an individual's risk for various common, complex medical disorders. Consequently, genetic testing is becoming an integral part of health care. There are now genetic tests available for close to 1,000 diseases or conditions, including hereditary breast cancer and cystic fibrosis, and there is great potential for future test development and use.

However, only about a dozen[2] genetic tests have been reviewed and approved by the Food and Drug Administration (FDA) to ensure their safety and effectiveness. A major reason is that the FDA regulates the safety and effectiveness of medical devices, meaning products intended to diagnose, treat, mitigate, or prevent disease.[3] A genetic test is considered by the FDA to be a medical device only if it is manufactured as a freestanding "kit" and sold to a laboratory.[4] Presently, though, most genetic tests are not sold as kits but are manufactured in-house by clinical laboratories.[5] In these cases, the laboratory itself decides whether a test has sufficient "clinical validity" (i.e., is sufficiently effective at measuring what it purports to measure). Although all clinical laboratories must be approved under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and meet general standards applicable to all laboratories, there is no genetic testing specialty under CLIA. This means that there are

[1]DNA stands for deoxyribonucleic acid.

[2]These include tests for cystic fibrosis; factor II and factor V Leiden, which affect blood clotting; cytochrome P450 genotyping, which affects the rate at which drugs are metabolized and thus can help in determining dosage; and Her-2 neu, which is used to determine whether a woman will benefit from a breast cancer drug called Herceptin.

[3]See 21 U.S.C. §§ 360c(f)(1), 360e(c)(1) and 21 C.F.R. pt. 809.

[4]21 U.S.C. § 321(h).

[5]See 61 Fed. Reg. 10, 484.

no specific requirements or unique standards for laboratories that perform genetic tests.[6]

This minimal oversight makes it difficult for consumers to determine whether a genetic test provides meaningful, scientifically based information. In fact, some companies are directly marketing to consumers DNA tests that provide health-related information without the advice of a physician, including so-called "nutrigenetic" tests. Nutrigenetic tests purport to analyze a limited number of genes to provide personalized nutritional and lifestyle recommendations. These tests, which have not been approved by the FDA and are sometimes performed in laboratories that have not been approved under CLIA, range in cost from under $100 to over $1,000. The tests require consumers to self-collect a sample of genetic material, usually from a cheek swab, and then forward the sample to a laboratory for analysis. Demand for this type of service appears to be on the rise; one company estimates that it has sold over 35,000 nutrigenetic tests to consumers since it began selling the tests in the United States in 2003.

Although the companies that market nutrigenetic tests typically stress that the results and information they provide are not intended to diagnose or treat any disease or disorder, they do claim that their tests will provide consumers with the information needed to tailor their diet and exercise programs to address their genetically determined health risks. Because of your concerns that the companies marketing this type of test may be misleading consumers by providing inaccurate information, you requested that we investigate the "legitimacy" of these claims.

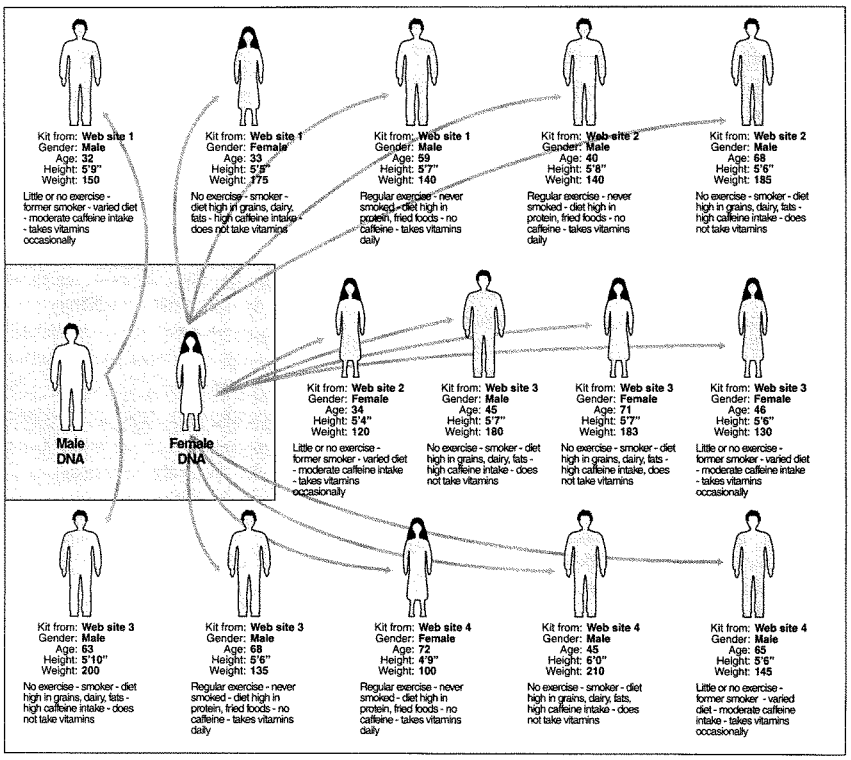
To complete our work, we investigated a nonrepresentative selection of four Web sites selling nutrigenetic tests. We chose these Web sites because they all claimed that their tests would analyze a limited number of genes, between 4 and 19, to create personalized dietary and other lifestyle-related recommendations; they also stated that their products would not test for disease or predisposition to disease. These tests ranged in price from $89 to $395. We purchased several similar types of tests from each site—14 in total—so that we could compare a variety of results. To create a testing scenario, we developed a series of "fictitious consumers." To do this, we ultimately submitted 12 DNA samples taken by cheek swab from a 9-month-old female, with consent from her parents. For comparison

[6]See Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263(a).

purposes, we also submitted 2 DNA samples taken from an unrelated 48-year-old male. We had originally submitted DNA samples taken from a dog, a cat, and "blank" samples containing no DNA information, but these submissions were returned to us because they could not be processed by the laboratories.

On questionnaires that were included with each of the tests, we described the DNA from the female and the DNA from the male as coming from adult men and women of various ages, weights, and lifestyle descriptions. Each questionnaire asked for the same type of information about exercise, smoking, vitamin consumption, and intake of a variety of foods, but did not ask for information about current medical conditions or prescribed medications being taken. Figure 1 provides the basis for the 14 fictitious consumers we created.

Figure 1: DNA and Lifestyle Descriptions Used to Create 14 Fictitious Consumers



Source: GAO.

To assess whether the 14 results and related recommendations we eventually received provided any scientifically-based information, we consulted with outside experts in the fields of genetics and nutrition.

These experts have background in a variety of areas related to both fields, including genetic technology, genetic discrimination, legal and public policy issues pertaining to genetics and human research, pediatrics, prevention of communicable diseases and diseases associated with poor nutrition, and defining global nutrient requirements. We also reviewed recent studies on genetic links to specific diseases and on the efficacy of nutritional supplements. In addition, we interviewed representatives from the Web sites marketing the tests and the laboratories processing the results. We conducted our investigation from August 2005 through June 2006 in accordance with quality standards for investigations as set forth by the President's Council on Integrity and Efficiency.

Summary

The results we received from all the tests we purchased mislead the consumer by making health-related predictions that are medically unproven and so ambiguous that they do not provide meaningful information to consumers. Although the results contain statements indicating that the information provided is not intended to diagnose disease or predisposition to disease, all of the 14 results we received do contain predictions that a consumer may interpret as diagnoses. For example, the 14 results indicate that our fictitious consumers are at risk for developing a range of conditions, including osteoporosis, high blood pressure, type 2 diabetes, heart disease, a reduced ability to clear toxins, brain aging, and cancer. The 3 results we received from the tests we purchased from Web site 4 also stated that our fictitious consumers were at *below average* risk for developing certain medical conditions. Experts informed us that although some types of diseases, such as cystic fibrosis, can be definitively diagnosed by looking at specific genes, the kinds of predictions we received cannot be proven given the level of scientific evidence available today. Even if the predictions could be medically proven, the way the results are presented renders them meaningless. For example, many people "may" be "at increased risk" for developing heart disease because of a variety of factors, so such an ambiguous statement could apply to any human that submitted DNA.

Results from the tests that we purchased from Web sites 1 and 4 further mislead the consumer by recommending costly supplements that they claim are developed according to an individual's unique DNA. In reality, the pills are not unique in any way, make unproven medical claims, and are potentially harmful. For example, the 3 results we received from the tests from Web site 1 encourage the purchase of "personalized" dietary supplements, supposedly formulated based on our fictitious consumers' DNA and lifestyle profiles, and costing approximately $1,200 per year.

However, when we examined the lists of ingredients, we found that the pills do not appear to be customized because the 3 fictitious consumers we created for this Web site received recommendations to purchase the same product, despite the fact that there were 2 different DNA donors and each had a different lifestyle profile. Moreover, experts confirmed that these supplements are substantially the same as typical multivitamins that can be found in any grocery store for about $35 per year. In addition, the 3 results we received from the tests we purchased from Web site 4 claimed that for over $1,880 per year, its "unique" and "personalized" products could repair damaged DNA. The experts we spoke with stated that there is no "pill" currently available that has been proven to do so. Again, these supplements do not appear to be personalized because the 3 fictitious consumers we created for this site received the same recommendation. Finally, the experts we spoke with told us that in some circumstances, taking supplements such as those that were recommended to us can be harmful. For example, taking levels of some vitamins and nutrients that exceed the recommended daily allowance may promote cancers and chronic diseases.

Furthermore, results from the tests that we purchased from Web sites 1, 2, and 3 do not provide dietary and lifestyle recommendations based on a unique genetic profile as promised. Instead, the recommendations we received simply provide generally accepted health advice directly linked to information we submitted via the questionnaires included with the tests. If the recommendations were truly based on a consumer's unique genetic profile, then the 9 fictitious consumers that we created for Web sites 1, 2, and 3 using the female DNA should have received the same recommendations. Instead, these 9 consumers received a variety of different recommendations, depending on the fictitious lifestyles we provided for them. For example, if we said the consumers smoked, we received recommendations to stop smoking. In contrast, if we said that the consumers never smoked, we received recommendations to continue to avoid smoking. These results lead us to conclude that we could have invented any type of lifestyle description for the DNA we submitted and the recommendations would simply echo this information. Although these recommendations may be beneficial to consumers in that they constitute common sense health and dietary guidance, DNA analysis is not needed to generate this advice.

During the course of our investigation, we found other information that raises concerns for consumers purchasing these tests. For example, we discovered that Web sites 1, 2, and 3 were in fact selling the same genetic test developed by the same company, and that this company was

pressured by consumer groups in the United Kingdom to stop selling the test in that country. The company now sells the same type of test in the United States. In addition, we found evidence suggesting a lack of quality control by the laboratory actually conducting the DNA analysis for Web sites 1, 2, and 3. For example, even though all of the genetic information contained in the test results based on a single source should be identical, we received disparate results for a sample from the same source from the tests we purchased from Web site 1. We also found that a laboratory used by Web site 4 is not approved under CLIA.

Results Contain Health-related Predictions That Are Both Medically Unproven and Meaningless

Although there are numerous disclaimers indicating that the tests we purchased do not diagnose disease, the 14 results we received predicted that our fictitious consumers were at risk of developing a myriad of medical conditions. These predictions were similar for all of our fictitious consumers, no matter which DNA or lifestyle description we used. Results from the tests we purchased from Web site 4 also stated that our fictitious consumers were at *below average* risk for developing certain diseases. However, after consulting with outside experts, we determined that these predictions cannot be medically proven at this time. Even if the predictions could be medically proven, the results use ambiguous language to describe the supposed health risks, rendering them meaningless.

Claims That Test Results Will Not Diagnose Disease

As shown in table 1, the results we received from the tests we purchased from all four Web sites contain statements indicating that the information they provide is not intended to diagnose disease or predisposition to disease. The results also contain language stressing that the tests do not screen for genetic disorders and advising consumers to consult with a physician if they feel that they might be ill.

Table 1: Claims That Test Results Are Not Intended to Diagnose Disease

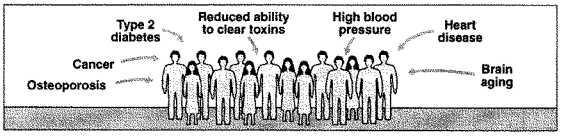
Tests purchased from	Selected disclaimers
Web site 1	[This is] not a genetic test for disease or predisposition to disease, nor does it determine a medical condition. If you think you may be ill, consult your doctor.
Web site 2	Please note that this screening is not a test for inherited disorders.
Web site 3	[This is] not a genetic test for disease or predisposition to disease, nor does it determine a medical condition. If you think you may be ill, consult your doctor.
Web site 4	[Our] products are not intended to diagnose or treat any disease or disorder; only your doctor can do so.

Source: GAO.

Predictions of Medical Conditions Received

Despite these statements, the results we received from the tests we purchased from all four Web sites do contain medical predictions that a consumer may interpret as diagnoses. The overriding impression from all the results is that the 14 fictitious consumers we created are at risk for developing a variety of medical conditions, as shown in figure 2.

Figure 2: Medical Conditions Predicted for 14 Fictitious Consumers



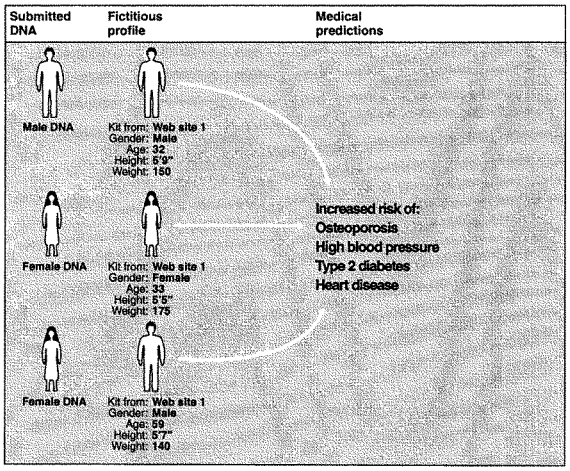
Source: GAO.

Furthermore, the results from the tests we purchased from Web site 4 even suggested that our fictitious consumers with the female DNA were at *below average* risk for developing certain conditions. As comparison, the 2 results we received from Web sites 1 and 3 for the fictitious consumers with the male DNA contained similar predictions, despite having different DNA variants from the female sample. Specific predictions from each test are discussed in further detail below.

With regard to the tests we purchased from Web site 1, the 3 results we received stated that the DNA sample from the female displayed an "increased risk of reduced calcium and Vitamin D absorption," meaning

that she "may be at increased risk of developing osteoporosis." Results from the same tests contained similar predictions with regard to risks for developing high blood pressure, type 2 diabetes, and heart disease. The DNA sample from the male that we submitted for this test showed the exact same risks, despite having different DNA variants from the female, as shown in figure 3.

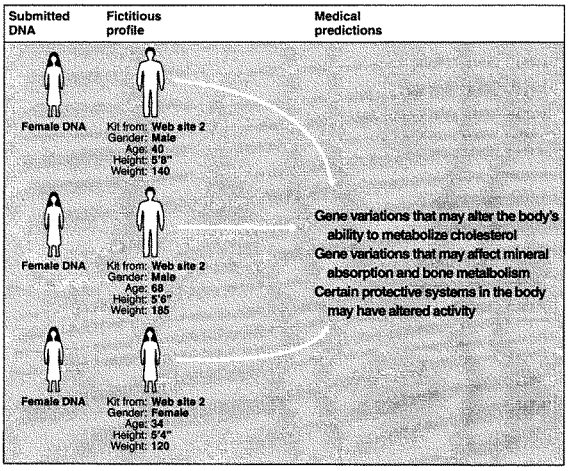
Figure 3: Predictions Received from the Tests Purchased from Web Site 1



Source: GAO.

As shown in figure 4, the 3 results from the tests we purchased from Web site 2 stated that the DNA sample from the female showed "gene variations that may alter the body's ability to metabolize cholesterol" and variations that may affect "mineral absorption and bone metabolism." These results also suggested that "certain protective systems" in the body "may have altered activity."

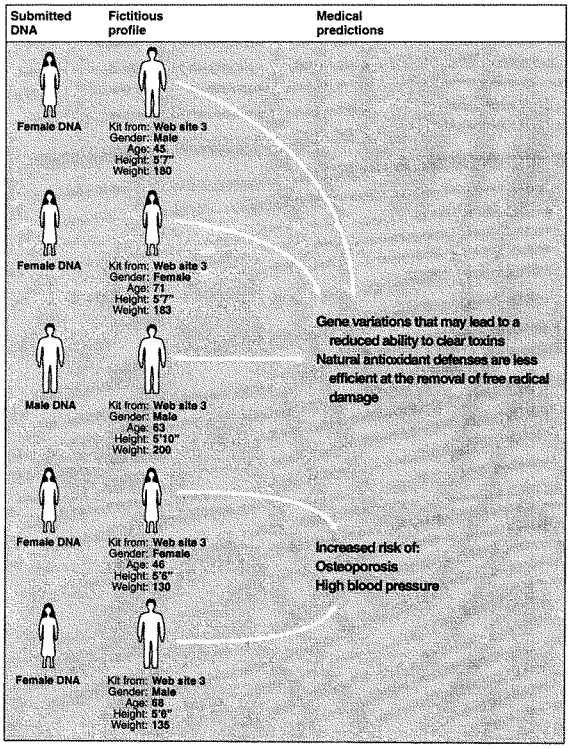
Figure 4: Predictions Received from the Tests Purchased from Web Site 2



Source: GAO.

Of the 5 tests we purchased from Web site 3, 3 focused on detoxification, 1 focused on heart health, and 1 focused on bone health. The 5 results thus showed a range of predictions, including that the DNA from the female contained gene variations that "may lead to a reduced ability to clear toxins" and that her "natural antioxidant defenses are less efficient at the removal of free radical damage." The results also showed increased risk of high blood pressure and osteoporosis. The DNA we submitted from the male showed similar risks with regard to toxins and removal of free radicals, despite having different DNA variants from the female sample. See figure 5.

Figure 5: Predictions Received from the Tests Purchased from Web Site 3

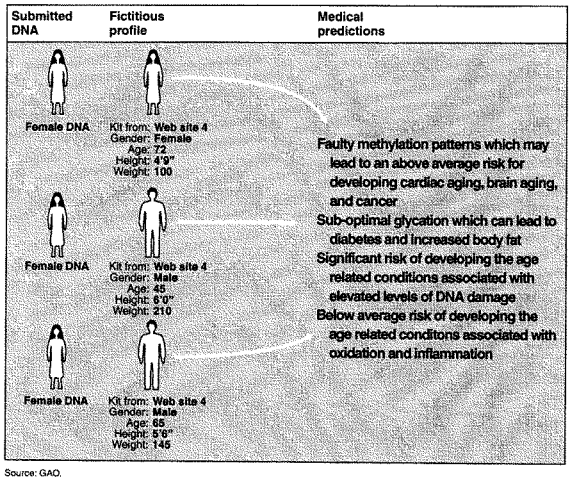


Source: GAO.

Note: Of the five tests we purchased from Web site 3, three focused on detoxification, one focused on heart health, and one focused on bone health.

As shown in figure 6, the 3 results from the tests we purchased from Web site 4 showed that the DNA sample from the female revealed "faulty methylation patterns" which may lead to "an above average risk for developing cardiac aging, brain aging, and cancer" and "sub-optimal glycation," which can lead to diabetes and increased body fat. These same results also stated that the DNA displayed a "significant risk of developing the age related conditions associated with elevated levels of DNA damage." Results from the tests we purchased from Web site 4 also contain predictions that the DNA sample from the female shows relatively low risk for developing some diseases. For example, all the results from these tests note that the DNA displayed a "below average risk" of developing "the age related" conditions associated with "oxidation" and "inflammation." According to the results, oxidation can lead to diabetes, heart disorders, and Alzheimer's disease and inflammation can lead to diabetes, heart failure, and fragile bones.

Figure 6: Predictions Received from the Tests Purchased from Web Site 4



Source: GAO.

Predictions of Medical Conditions Cannot Be Medically Proven

Despite the implication that these predictions are based on the DNA submitted, none of the results we received contained scientific support to assist the consumer in evaluating their credibility, and there is no evidence to suggest that the tests have been evaluated by independent experts. Furthermore, the genetic experts we spoke with informed us that even though it is possible to make a definitive diagnosis of disease by looking at certain genes, none of the predictions contained in any of the results we received can be medically proven at this time. According to the experts, cystic fibrosis and Huntington's disease are examples of illnesses that can be diagnosed based on an analysis of only one gene.[7] In contrast, the diseases and conditions identified in the test results we received involve complex bodily processes. According to the experts we spoke with, although genes are known to be associated with these processes, scientists have very limited understanding about the functional significance of any particular gene, how it interacts with other genes, and the role of environmental factors in causing disease.

With regard to the specific predictions of heart disease, diabetes, osteoporosis, cancer, altered ability to metabolize cholesterol, and reduced ability to clear toxins, the experts informed us that research proving a genetic connection to the development of these conditions is at a very early stage and there are many issues yet to be resolved.

In addition, the experts we spoke with also stated that the types of tests we purchased cannot be used to confirm that an individual has a reduced risk of developing these types of diseases. Therefore, the claims that a person may be at "below average risk" of developing certain "age related conditions" based on the analysis of a few genetic variants is misleading. There could be other genetic variants not tested for that confer risk or other environmental factors not assessed.

Medical Predictions Are Also Meaningless

Even if the predictions could be medically proven, the way the results are presented—using ambiguous language—renders them meaningless. For example, it is unclear what is meant by a "damaged" gene. According to the experts we spoke with, although a specific gene can be "damaged" in that it contains a variation that causes a loss of function or impaired

[7]Cystic fibrosis is an incurable disease that causes mucus to build up in the body. People who have cystic fibrosis can have serious breathing problems and lung disease. Huntington's disease is a rare condition that causes parts of the brain to break down, or degenerate, causing rapid, jerky movements and dementia.

function, the results do not clearly explain what this means. The experts also told us that informing someone that they may be at increased risk for heart disease or that they have "high levels of DNA damage," "faulty methylation patterns," or "altered activity" in certain genes are all statements that are so ambiguous as to be meaningless. In fact, these types of predictions could apply to any human that submitted DNA. For example, according to the experts, many people "may" be "at increased risk" for developing heart disease because of known and unknown genetic risk factors; environmental and behavioral risk factors such as obesity, smoking, and high cholesterol; and the interaction between these genetic, environmental, and behavioral factors.

Results Encourage the Purchase of Supplements That Are Overpriced, Make Unproven Medical Claims, and May Even Be Harmful

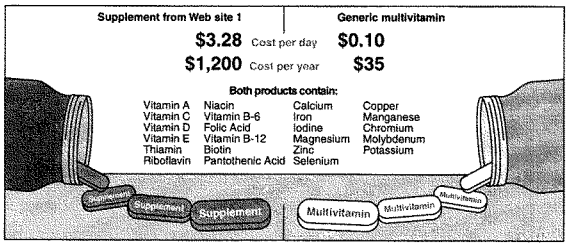
Results from the tests that we purchased from Web sites 1 and 4 further mislead the consumer by recommending expensive supplements. The 3 results we received from the tests we purchased from Web site 1 recommend a supplement that is supposedly based on an individual's unique DNA; in reality, the supplements are not unique and are simply a grossly overpriced version of a typical multivitamin. The 3 results we received from the tests we purchased from Web site 4 similarly recommend expensive supplements that are supposedly unique to the consumer; these results also contain medical claims about the supplements that cannot be proven at this time. Finally, the experts we consulted informed us that, in some instances, taking certain supplements may be harmful.

Supplements Recommended by the Tests Purchased from Web Site 1

The results from the tests we purchased from Web site 1 recommended a 90-day supply of a "personalized, custom" nutritional formula for $295, or approximately $1,200 per year. According to the product information, this formula is based on "what your genetic profile reveals as areas in your body that may need special support." Despite this claim, when we examined the listed ingredients, we found that we were recommended the same product for all 3 of the fictitious consumers we created for this test—2 of these consumers actually had the DNA from the female, 1 had the DNA from the male, and all 3 had different lifestyle descriptions, as previously shown in figure 1. However, when we compared the contents of the supplements recommended for the 2 fictitious consumers with DNA from the female with the supplement recommended for the fictitious consumer with DNA from the male, we found that the ingredients were the same.

Moreover, the experts we spoke with confirmed that the supplements themselves are not unique; they contain vitamins that can be found in any pharmacy or grocery store. To find a comparable product, we went to a local drug store and found a generic multivitamin with the same ingredients, though with different amounts, as those in the recommended supplement. In contrast to the exorbitant price requested for the supplement, we paid just under $10 for a 100-day supply of this multivitamin—or about $35 per year, as shown below.

Figure 7: Comparison of Recommended Supplement from Web Site 1 with Generic Multivitamin



Source: GAO.

Although these products are not identical, the experts we spoke with said that both the supplement and the generic vitamin would probably provide the same nutritional benefits for most people. However, they also cautioned that the elevated amounts of certain vitamins in the supplement may be harmful, as discussed later in this testimony.

Supplements Recommended by the Tests Purchased from Web Site 4

The results from the tests we purchased from Web site 4 recommended a "personalized" supplement "regimen" costing over $1,880 per year. According to the results, these supplements are personalized based on the DNA submitted and lifestyle descriptions provided on the questionnaires, and they are supposed to help "compensate" for "genetic deficiencies." Specifically, the product information accompanying the test results claims that the regimen will repair damaged DNA through the consumption of 7 pills per day, including

- 4 tablets per day of a supplement containing over "70 vitamins, minerals, and enzymes combined with "CAEs", a proprietary extract from the Tropical Rainforest botanical Uncaria tomentosa, known as Cat's Claw, which has been clinically shown to promote DNA repair in the body." A 60-day supply costs $160.
- 1 tablet per day of a supplement designed to "enhance the body's ability to repair damaged DNA." A 60-day supply costs $50.
- 1 tablet per day of a supplement to control blood sugar and body fat. A 60-day supply costs $50.
- 1 tablet per day of a supplement designed to manage the process "whereby certain genes are activated and deactivated." A 60-day supply costs $50.

As with the other products we were recommended, these supplements are not unique to the consumer. Although the 3 fictitious consumers we created for this site in reality all had the female DNA, they all had varying lifestyle descriptions, as previously shown in figure 1. However, we received the same product recommendation for all 3 consumers. For example, our fictitious 72-year-old female nonsmoker with a diet high in protein was recommended the same supplement regimen as our fictitious 45-year-old male smoker with a diet high in fats, which seems illogical given that the supplements are supposedly developed based in part on the submitted lifestyle information.

Furthermore, although the regimen touts "Cat's Claw" as being the ingredient primarily responsible for DNA repair, the experts we spoke with told us that these claims are not medically proven at this time. According to the experts, Cat's Claw is a plant whose pharmacological properties are being studied for a wide variety of biological effects, but the experts were aware of no reports in peer-reviewed scientific literature that have demonstrated the ability of Cat's Claw to repair DNA. Furthermore, although there is some research indicating that taking antioxidants may help with DNA repair, no pill has yet been proven to repair damaged DNA. In fact, manufacturers of supplements are prohibited from claiming that their products can treat, cure, or prevent disease; products that make these claims are considered drugs and must be approved by the FDA before they can be sold. The FDA has already sent Warning Letters to several dietary supplement manufacturers who explicitly claimed that Cat's Claw could help treat cancer and arthritis. However, we do not know whether the FDA would consider a claim of "DNA repair" to render Cat's Claw an unapproved drug.

Nutritional Supplements May Also Be Harmful

Regarding safety, the nutritionists we spoke with said that it is possible that improper use of dietary supplements can be harmful. For example, the nutritionists said that taking levels of some vitamins and nutrients that far exceed the recommended daily allowance[8] may promote cancers and chronic diseases. A recent statement issued by the National Institutes of Health[9] also notes that taking more than the recommended daily intake of certain vitamins and minerals may cause adverse health effects. For example, smokers who consume excessive amounts of beta-carotene may be at increased risk for developing lung cancer, while consumption of excessive amounts of vitamin D and calcium may increase the risk of kidney stones. Furthermore, we were told that all nutrients or "food components" can be toxic if provided in sufficient quantities, but the susceptibility to toxicity varies among the population. For example, there is evidence that some people may be at risk because of excessive intakes of vitamin E, folic acid, calcium, or selenium.

When we asked the nutritionists about the safety of specific ingredients in the supplements recommended for our fictitious consumers, they generally believed that the supplements were comparable to typical multivitamins, as previously stated. However, they also expressed a variety of concerns. For example, one of the nutritionists we consulted characterized the levels of vitamin B-6 in both products as "disturbing." Another felt that the levels of Vitamin A in both were "high," and that the supplements from Web site 1 contained excessive amounts of iron, because iron stays in the blood and could become toxic. Other experts told us that the supplements could be harmful if taken in combination with certain medications. For example, Cat's Claw may have an adverse interaction with a medication prescribed for people who are at increased risk for forming blood clots, and individuals taking this medication are advised to avoid all supplements unless a physician approves.

[8]See http://dietary-supplements.info.nih.gov for detailed information on recommended daily allowances.

[9]National Institutes of Health, *State-of-the-science Conference Statement: Multivitamin/Mineral Supplements and Chronic Disease Prevention*, May 15–17, 2006.

Results Do Not Provide Recommendations Based on a Unique Genetic Profile

Results from the tests that we purchased from Web sites 1, 2, and 3 promise recommendations based on the consumer's unique genetic profile. However, the 11 results we received from these three sites suggest that the DNA submitted was not a factor in determining the recommendations. Rather, the results simply provide a number of common sense health recommendations based on information we submitted on the lifestyle questionnaires.

Tests Promise Unique Recommendations

Although Web sites 1, 2, and 3 acknowledge that information submitted on the questionnaires is taken into consideration when determining diet and lifestyle recommendations, the overall implication to the consumer is that the information derived from the DNA analysis is the most important factor, as shown in table 2.

Table 2: Statements Promising Recommendations Based on Consumers' Unique Genetic Information

Tests purchased from	Product Claims
Web site 1	• "Recommendations are based on your own DNA." • By "adjusting your diet and lifestyle to your genetic profile, you can make sure that your body functions at an optimum level."
Web site 2	• "Recommendations are based on the unique combination of your genetic makeup" because it is important to "make lifestyle choices" that match your genes.
Web site 3	• "Recommendations are based on your own DNA." • Recommendations will "focus on gene variations, the potential of which may be offset by eating certain foods, increasing the intake of specific micronutrients, or making lifestyle changes."

Source: GAO.

Results Instead Provide Recommendations Based on Information Submitted on Questionnaires

Despite these claims, the recommendations we received are simply common sense regimens directly linked to the information we submitted on the questionnaires included with each test. For example, 9 of the 11 consumers we created for Web sites 1, 2, and 3 had the female DNA. If the recommendations were truly based on the consumer's unique genetic profile, then these 9 consumers should have received the same recommendations because their DNA came from the same source. Instead, they received a variety of different recommendations, depending on the fictitious lifestyles we provided for them. For example, when we said that

a fictitious consumer with the female DNA smoked and ate a lot of fatty foods, we received recommendations to stop smoking and eat fewer fatty foods. In contrast, when we said that another fictitious consumer with the female DNA never smoked and did not eat a lot of fatty foods, we received recommendations to continue to avoid both smoking and eating foods high in fat. Similarly, when we said that fictitious consumers with the female DNA did not eat a lot of fruits and vegetables, we received recommendations to eat more of these foods. However, if we said that the consumer had a diet rich in fruits and vegetables, we were told to continue this high level of consumption.

We received similar recommendations with regard to the 2 remaining consumers we created using the male DNA. For example, for one of the fictitious consumers with this DNA, we provided a lifestyle description stating that the consumer ate only moderate levels of leafy green vegetables, cantaloupe, and eggs—foods that are rich in antioxidants. In this case, the consumer was told to eat more foods rich in antioxidants. In contrast, we said that the other consumer with the male DNA ate a lot of antioxidant-rich foods. This time, we received recommendations to continue high consumption of these foods. Figure 8 provides further examples of the relationship between the lifestyle information we submitted on the questionnaires and the recommendations we received.

Figure 8: Lifestyle Descriptions Directly Linked to Diet and Health Recommendations

Submitted DNA	Fictitious profile	Submitted lifestyle information	Lifestyle recommendations
Male DNA	Kit from: **Web site 1** Gender: **Male** Age: **32** Height: **5'9"** Weight: **150**	Little or no exercise Former smoker Diet low in food containing Omega-3 fatty acids and calcium Moderate caffeine intake	Increase exercise Continue to avoid smoking Increase intake of Omega-3 fatty acids Increase calcium intake Decrease caffeine consumption
Female DNA	Kit from: **Web site 2** Gender: **Male** Age: **40** Height: **5'8"** Weight: **140**	Regular exercise Never smoked Diet high in cruciferous vegetables (broccoli, cauliflower, turnips) Diet high in fried foods	Continue to exercise Continue to avoid smoking Continue consumption of cruciferous vegetables Decrease total fat intake
Female DNA	Kit from: **Web site 3** Gender: **Female** Age: **71** Height: **5'7"** Weight: **183**	No exercise Smoker Diet high in carbohydrates Diet high in fats	Increase exercise Stop smoking Reduce intake of refined carbohydrates Reduce saturated fats

Source: GAO.

These results lead us to conclude that we could have invented any type of lifestyle description for the DNA we submitted and the recommendations would simply echo this information. Although these recommendations may be beneficial to consumers in that they constitute common sense health and dietary guidance, DNA analysis is not needed to generate this advice.

Other Investigative Findings Raise Concerns

During the course of our investigation, we found other information that raises concerns for consumers purchasing these tests. For example, we discovered that Web sites 1, 2, and 3 were in fact selling the same genetic test developed by the same company and that this company was pressured by consumer groups in the United Kingdom to stop selling the test in that country. The company now sells the same type of test in the United States. In addition, we found evidence suggesting a lack of quality control by the

laboratory actually conducting the DNA analysis for Web sites 1, 2, and 3. For example, even though all of the genetic information contained in the test results based on a single source should be identical, we received disparate results from the tests we purchased from Web site 1. We also found that the laboratory used by Web site 4 is not approved under CLIA.

Nutrigentic Testing in the United Kingdom: The company that manufactures the tests used by Web sites 1, 2, and 3 used to sell the same type of test in the United Kingdom—consumers provided DNA samples and filled out a lifestyle questionnaire, and the company provided advice on what consumers should do to improve their health with diet and lifestyle changes. The Human Genetics Commission, the U.K.'s strategic advisory body on developments in human genetics, and GeneWatch UK, a consumer protection group, alleged that the company's tests were misleading because no scientific evidence validated their clinical claims. Other scientists and consumer protection groups also cited numerous problems with the tests, including that the claims were exaggerated, the service should not be offered without adequate counseling, and that they provided advice which differed little from standard guidance on diet and exercise.

Eventually, the tests were subjected to assessment by a team of three experts—a clinical geneticist, a scientist leading a program of research in nutritional genomics, and the chief dietitian of a leading teaching hospital. They published the findings in a detailed report that concluded that there was no value in the genetic tests being offered. Subsequently, GeneWatch U.K. raised these concerns with major retail chains and pharmacies carrying the tests and urged them to stop selling the tests. By July 2002, the company was no longer attempting to sell their test directly to the consumer in the United Kingdom, either over the Internet or through retailers. In 2003, the company moved its operations from the United Kingdom to the United States. Despite the findings of the British experts, the company now sells the same type of test to American consumers.

Contradictory DNA Analysis: The results we received from the tests we purchased from Web site 1 appear to be contradictory and reflect inaccurate lab results. Specifically, the results we received from these tests contained a listing of the genes being analyzed and any "variations" found in those genes. When we compared the two results we received based on the DNA from the female, we found that the gene variations listed were not exactly the same: one result said that the DNA showed a variation in the "eNOS" gene, but the other result said that there was no variation in this gene. According to the experts we spoke with, because

the DNA sample was taken from the same individual, any gene variations should be identical. The experts also stated that a competent laboratory should reliably be able to detect the presence or absence of a particular gene variant. Consequently, concerns exist about whether this laboratory has basic quality control procedures in place to identify and prevent mistakes.

Lack of CLIA Approval: As noted in the introduction to our testimony, laboratories performing genetic tests for medical purposes must be approved under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). In general, CLIA regulations address personnel qualifications, quality control and assurance, recordkeeping requirements, and also require laboratories to conduct proficiency testing. All laboratory tests performed to provide information about an individual's health must be conducted by law in approved laboratories. During the course of our work, when we interviewed a representative from a laboratory conducting tests for Web site 4, we were told that this lab is not approved under CLIA.

Conclusion

The current regulatory environment provides only limited oversight to those developing and marketing new types of genetic tests. Consequently, companies that sell nutrigenetic tests like the ones we purchased may mislead consumers by promising results they cannot deliver. Further, the unproven medical predictions these companies can include in their test results may needlessly alarm consumers into thinking that they have an illness or that they need to buy a costly supplement in order to prevent an illness. Perhaps even more troubling, the test results may falsely assure consumers that they are healthy when this may not be the case.

With further advances in science, nutrigenetic tests like those we purchased may in the future be valid, allowing consumers to use DNA-based analysis to make diet and lifestyle changes that will actually prevent the development of disease. However, as demand for these new tests continues to rise, it will become increasingly important for consumers to have reliable information in order to determine which tests are accurate and useful.

Mr. Chairman and Members of the Committee, this concludes my statement. I would be pleased to answer any questions that you or other members of the committee may have at this time.

Contact

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The CHAIRMAN. Thank you very much, Greg.

Kathy Hudson.

STATEMENT OF KATHY HUDSON, DIRECTOR, GENETICS AND PUBLIC POLICY CENTER, AND ASSOCIATE PROFESSOR, BERMAN BIOETHICS INSTITUTE, INSTITUTE OF GENETIC MEDICINE AND DEPARTMENT OF PEDIATRICS, JOHNS HOPKINS UNIVERSITY, WASHINGTON, DC

Dr. HUDSON. Thank you, Mr. Chairman, and thank you for inviting me to testify today and for focusing your attention on this important topic that has consequences for people of all ages.

I would like to begin by saying unequivocally that genetic testing today is having a documented beneficial impact on clinical care and holds enormous promise for future improvements. Today, there are genetic tests clinically available for nearly 1,000 different diseases and hundreds more in development.

Genetic tests provide information, information that can be used to diagnose disease, to predict risk of future disease, and to guide decisions about whether to undergo a medical procedure or to take a particular dose of drug or a particular drug. Genetic tests lead to critical health and life decisions, and therefore it is imperative that this information be accurate and reliable and relevant to an individual's health.

While many genetic tests available today are of extraordinary quality, inadequacies in the current oversight of genetic testing identified by the GAO and studies by my Center threaten more than the public's pocketbook; they threaten the public's health. For a genetic test to be of high quality, it must be analytically valid as well as clinically valid. Analytic validity refers to a laboratory's ability to get the right answer reliably over time, to detect a genetic variation when it is present, and, importantly, not to detect it when it is not present. Clinical validity refers to the relationship of a genetic mutation to a specific health outcome.

Current regulations fail to ensure either analytic or clinical validity of genetic tests. The responsibility for ensuring the analytic validity of genetic tests lies with the Centers for Medicare and Medicaid Services, CMS, as you mentioned, which is responsible for implementing the Clinical Laboratory Improvement Amendments of 1988.

In enacting CLIA, Congress believed that proficiency testing, or external validation of a laboratory's performance, was, and I quote, "testing should be the central element in determining a laboratory's competence, since it purports to measure actual test outcomes rather than merely gauging the potential for accurate outcomes." Unfortunately, 18 years after enacting the laboratory amendments, problems persist and are particularly acute in the genetic testing arena.

Despite the recommendations of government advisory committees, CMS has failed to create specific proficiency testing standards for genetic tests. While some laboratories maintain accuracy of their testing procedures by voluntarily enrolling in programs for proficiency testing, others do not. Immediate action by CMS is urgently needed to create proficiency testing standards for genetics under CLIA. In November of last year, my center called on CMS

to issue these regulations expeditiously, and subsequently nearly a hundred groups, including patients, health care providers, industry and women's health advocates, have added their voices and called on CMS to act.

The GAO reports real errors occurring in genetic testing laboratories. The GAO submitted a DNA sample from a single individual for testing under different assumed identities. Even though the DNA was identical, the test results were not. This should disturb us all.

Testing errors have real consequences for real people, and enhancements in CLIA could make a real difference. A recent survey by my center showed that higher levels of participation in a proficiency testing program is correlated with a reduction in errors. So we need to increase proficiency testing and we need to enhance CLIA.

Even if CLIA were to operate perfectly, there would still be problems, and that is because CLIA is focused on analytic validity and laboratory quality and not on the clinical validity. What is the relationship between the DNA mutation and health? Does it cause cancer, does it cause diabetes, et cetera?

Currently, there is no government agency with clear responsibility to ensure clinical validity of most tests. Therefore, each laboratory director makes an independent decision regarding whether tests have sufficient validity to be offered to the public. As I said, many laboratories are of extraordinarily high quality and offer only tests for which there is broad scientific agreement regarding the clinical validity. But several reports, notably the GAO report, indicate that laboratories are offering tests to the public in the absence of sufficient evidence of their clinical validity. Moreover, because there is no requirement that laboratories disclose the scientific basis for their test, it is not possible for consumers to determine whether a test is bogus or based in real science.

Some have recommended that the Food and Drug Administration step in here and ensure the clinical validity of some or all genetic tests. Currently, FDA regulates only a small handful of these tests, those that are marketed as test kits. FDA has sent very mixed signals over the years regarding its jurisdiction and willingness to regulate home brews.

As a result, we have a two-path system for regulation of genetic tests. Those companies that have invested time, money and effort to develop test kits face competition from clinical laboratories using home brews. This uneven regulatory playing field provides a disincentive for the development of test kits with clear clinical validity.

In conclusion, quality genetic testing requires good tests and competent laboratories. Current oversight assures neither. I want to applaud you, Mr. Chairman and the Committee, for taking the first steps in investigating questionable oversight and questionable genetic tests, and I urge you to continue to provide leadership in this area.

Thank you.

[The prepared statement of Ms. Hudson follows:]

Testimony of Kathy Hudson, Ph.D.
Director, Genetics and Public Policy Center
& Associate Professor, Berman Bioethics Institute,
Institute of Genetic Medicine & Department of Pediatrics
Johns Hopkins University

Before the United States Senate Special Committee on Aging

"At Home DNA Tests: Marketing Scam or Medical Breakthrough?"

July 27, 2006

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Mr. Chairman and Members of the Committee:

Thank you for inviting me to be here today to discuss the ethical, legal, and social concerns relating to direct-to-consumer clinical genetic testing. I appreciate the opportunity to share with you the results of the Center's work and our policy recommendations in this arena.

My name is Kathy Hudson and I am Director of the Genetics and Public Policy Center and Associate Professor in the Berman Bioethics Institute, the Institute of Genetic Medicine, and the Department of Pediatrics, at Johns Hopkins University. Established with a grant from The Pew Charitable Trusts, the mission of the Genetics and Public Policy Center is to provide independent and objective information and analysis on genetic technologies and genetic policies. We hope our work provides useful tools for decision makers as they respond to the challenges and opportunities arising from advances in human genetics.

I commend the Committee for focusing on this important topic and the GAO for undertaking an investigation of troubling commercial practices with respect to certain genetic tests being offered directly to consumers.

Today I would like to make four points. First, genetic testing is growing rapidly and holds great promise to improve health and health care. Second, the current system for oversight of genetic testing is inadequate. Third, gaps in oversight pose real threats to the public's health. And last, I would like to share some policy recommendations to fill those gaps and help ensure that the promise of genetics is realized.

Current Uses of Genetic Testing

There are many contexts in which genetic tests are used, including forensic testing, ancestry testing, and paternity testing. Consistent with the focus of the GAO investigation, my testimony today will focus only on health-related uses of genetic testing.

Genetic testing is becoming an increasingly important part of medical care. Once the province of esoteric testing laboratories and limited to rare diseases or conditions, genetic tests now are being offered by a growing number of clinical laboratories for an increasing number and variety of conditions or health risks. The number of tests has increased 10-fold over the last decade and continues to grow. Today, there are genetic tests clinically available for nearly 1000 diseases, with hundreds more in development.[1] Genetic tests can be performed at any stage of the lifecycle: on fetuses during pregnancy, newborn babies, children, and adults of all ages.

Genetic tests provide information -- information that can be used to diagnose disease, to predict risk of future disease, and to guide decisions about whether to undergo a medical procedure or take a particular drug or dosage of a drug. Increasingly, genetic testing will

[1] GeneTests, www.genetests.org.

be used routinely in medical care to alert us to future health risks and guide early prevention and intervention. Genetic testing also will be used to help doctors prescribe the right medicine at the right dose for individual patients, thus avoiding costly and sometime tragic adverse drug reactions. The information provided by genetic tests is used to make profound, sometimes life-and-death, decisions. It is therefore imperative that this information be accurate and reliable and relevant to a patient's health.

Gaps in the Regulatory Landscape

Inadequacies in the current oversight of genetic testing identified by the Center[2] and in the GAO report threaten more than the public's pocketbook -- they threaten the public's health. The current regulatory environment fails to ensure the quality either of the laboratories performing genetic testing or of the tests they are offering. While these gaps affect all genetic tests, the ramifications of the current gaps in oversight are particularly evident with respect to some of the tests being offered directly to consumers.

For a genetic test to be of high quality, it must be both analytically and clinically valid. Analytic validity refers to a laboratory's ability to get the correct answer reliably over time, for example, to detect a genetic variation when it is present and *not* detect it when it is absent. Clinical validity refers to whether a particular genetic variation is associated with an individual's current or future heath status. Patients and providers need to know what it means to detect a specific genetic variant and equally importantly what it means if a variant is not detected.

All of us carry many variations in our DNA sequences; many of these are of no known clinical significance. Establishing clinical significance requires scientific evidence that correlates a particular genetic change with a specific health outcome. Gaps in current oversight mean that neither the analytic nor the clinical validity of genetic tests is adequately ensured.

Analytic Validity: What's the Problem with CLIA

Responsibility for ensuring the analytic validity of genetic tests lies with the Centers for Medicare and Medicaid Services (CMS), which implements the Clinical Laboratory Improvement Amendments of 1988 (CLIA). Congress enacted CLIA to "strengthen federal oversight of clinical laboratories to assure that the tests results are accurate and reliable"[3] after Congressional investigations found significant problems in the quality of testing services being provided to the public. The major problems identified by Congress were "lax federal oversight and direction, lack of proficiency testing for many analytes, inconsistent criteria for acceptable laboratory performance, and improprieties by

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[2] Javitt G, Hudson K. Federal Neglect: Regulation of Genetic Testing. Issues Sci. Technol. 2006 Spring; 22(3):59-66; Javitt G, Stanley E, and Hudson K. Direct-to-Consumer Genetic Tests, Government Oversight, and the First Amendment: What the Government Can (and Can't) Do to Protect the Public's Health. Oklahoma Law Review (2004) 57: 251-302; Baruch S, Javitt G, Scott J, and Hudson K. Reproductive Genetic Testing: Issues and Options for Policymakers. Washington, DC: Genetics and Public Policy Center, 2004.

[3] H.R. Rep. No. 100-899, at 8 (1988).

laboratories in handling specimen samples."[4] Deficiencies were particularly apparent in cytological screening of pap smears for cervical cancer. Congress found that many laboratories were reporting false negative results. In other words, women with abnormal, and possibly cancerous, cells were being incorrectly informed that their pap smears were normal.[5]

Congress, in enacting the amendments to CLIA, directed the Secretary of HHS to issue standards for the certification of laboratories, in order "to assure that such laboratories will consistently perform tests in a valid and reliable manner."[6] Proficiency testing, i.e., "a method of externally validating the level of a laboratory's performance,"[7] was a key element of the Amendments. According to the legislative history, Congress believed that proficiency testing should be the central element in determining a laboratory's competence, since it purports to measure actual test outcomes rather than merely gauging the potential for accurate outcomes.[8] Congress found "a number of serious defects in the current system" for proficiency testing.[9]

Unfortunately, 18 years later, these problems persist, and the implementation of CLIA with respect to genetic tests in particular has lagged behind advances in technology.

CLIA prohibits a clinical laboratory[10] from accepting human specimens for analysis unless the laboratory has been issued a certificate. Obtaining a certificate, in turn, requires that CMS or a CMS-approved body accredit the laboratory.

CLIA regulations provide different levels of oversight depending on the "complexity" of a test. Test complexity is determined through an algorithm that takes into account a number of factors including the training and skill required to perform the test and to interpret the results correctly. Tests that are considered "high complexity" are subject to additional test-specific requirements that address issues such as the qualifications of laboratory personnel and that mandate the enrollment in CLIA-approved proficiency testing programs. These test-specific requirements are implemented through the creation of a "specialty area." CMS has created specialty areas for many types of tests, including Microbiology, Diagnostic Immunology, and Chemistry.

Genetic tests are considered high complexity. Unlike other high-complexity tests, however, CLIA has not created a specialty area for most genetic tests. This means that there are no specified quality control, personnel, or proficiency testing requirements

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[4] Id. at 16.
[5] Id. at 16-17.
[6] Id. at 27.
[7] Id. at 15.
[8] Id. at 28.
[9] Id. at 15.
[10] CLIA defines a clinical laboratory as a "facility for the biological, microbiological, serological, chemical, immuno-hematological, hematological, biophysical, cytological, pathological, or other examination of materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings." 42 U.S.C. § 263a(a).

mandated under the CLIA regulations for most genetic tests. While some laboratories maintain the accuracy of their testing procedures by voluntarily enrolling in programs for proficiency testing, others do not. In the absence of a genetic testing specialty, it is difficult for health care providers or patients to distinguish between those laboratories that are qualified to perform genetic testing and those that are not.

Several government bodies have identified the creation of a specialty area as integral to adequate government oversight of genetic testing. As early as 1995, the National Institutes of Health and Department of Energy together convened a government task force to review genetic testing in the United States and make recommendations to ensure the development of safe and effective genetic tests. The task force recommended, among other things, that genetic tests not become clinically available unless they had been demonstrated, through independent external review, to be clinically valid. In 2000, the Secretary's Advisory Committee on Genetic Testing (SACGT) issued a report in which it concluded that the current oversight of genetic tests was insufficient to ensure their safety, accuracy, and clinical validity.[11] Among its recommendations, the SACGT proposed that CMS develop a specialty area for genetic testing under CLIA, and that FDA should review all new genetic tests. Neither of these recommendations has been implemented. In 2000, the government announced its intent to develop a specialty area under CLIA.[12] Six years later, no proposal has been forthcoming.

The Genetics and Public Policy Center believes that immediate action by CMS is urgently needed to create proficiency testing standards for genetic testing under CLIA. In November 2005, the Genetics and Public Policy Center called on CMS Administrator Mark McClellan to issue a proposed rule for a genetic testing specialty. Subsequently, nearly 100 groups, comprising patients, industry, health care providers, and women's health advocates, have added their voices and called on the Administrator to issue the proposed regulation.[13]

The GAO report documents real errors occurring in genetic testing laboratories. The GAO submitted a single DNA sample for testing under different assumed identities and received disparate results. While the DNA was identical, the genetic test results were not, with one result indicating that a genetic variant was present and another indicating it was not. Such laboratory errors are simply not acceptable and, for many tests, downright dangerous. Other studies have similarly documented genetic testing laboratory errors.[14]

We believe that laboratory errors such as these could be mitigated by enhanced oversight. A recent study by the Genetics and Public Policy Center provides evidence that the creation of a genetic testing specialty will be an effective approach to reduce analytic errors. Our survey of U.S. genetic testing laboratories revealed a wide range of

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[11] Enhancing the Oversight of Genetic Tests: Recommendations of the SACGT (2000), available at http://www4.od.nih.gov/oba/sacgt/reports/oversight_report.pdf

[12] 65 Fed. Reg. 25928 (May 4, 2000).

[13] See http://www.rhtp.org/documents/CLIAlettertoCMSSecMcClellan.pdf; http://www.geneticalliance.org/ws_display.asp?filter=testing_ltr

[14] Libby E et al. False-negative Factor V Leiden genetic testing in a patient with recurrent deep venous thrombosis. Am. J. Hematol. 2006 Apr;81(4):284-9

laboratory practices with respect to proficiency testing. Moreover, the survey found that laboratories with higher levels of participation in proficiency testing also reported fewer laboratory errors, demonstrating that proficiency testing is integral to quality laboratory testing. These results suggest that creation of a genetic testing specialty and the associated proficiency testing standards will enhance laboratory accuracy. In addition, the survey found a high level of support among laboratory directors for the creation of a genetic testing specialty.

In April 2006, CMS placed the issuance of a proposed rule on its regulatory agenda,[15] and we are cautiously optimistic that a proposed regulation will soon be forthcoming.

In addition to the absence of a genetic testing specialty, there are two other significant problems with CLIA that I would like to bring to your attention. First, the Center has determined that at least some laboratories offering genetic testing do not have CLIA certificates. This finding is quite disturbing and means that these laboratories are not being held responsible for meeting even the basic standards for laboratory quality applicable to all clinical laboratories. The second problem is that information about which laboratories are CLIA certified is not readily accessible to the average consumer or health care provider making if difficult, if not impossible, for doctors and patients to choose quality laboratories. The Center believes that it is in the interest of both providers and patients for CMS to enforce its current regulations more aggressively and to make publicly available the CLIA certification status of all laboratories, including those offering genetic testing.

Clinical Validity

The CLIA statute is focused on laboratory quality, not clinical validity of tests. Currently, there is no government agency with clear responsibility to ensure the clinical validity of most genetic tests. Therefore, each laboratory director makes an independent decision regarding whether a genetic test has sufficient clinical validity for it to be offered to the public. Many laboratories are of extraordinarily high quality and offer only those tests for which there is broad scientific agreement regarding clinical validity. However, several reports, notably the new GAO report, indicate that some laboratories are offering genetic tests to the public in the absence of sufficient evidence of their clinical validity. Moreover, because there is no requirement that laboratories disclose publicly the scientific basis for their tests, it is not possible for consumers to determine whether a test is bogus or is based on real science.

Some have recommended that the Food and Drug Administration (FDA) take responsibility for ensuring the clinical validity of all or some genetic tests. Currently, FDA regulates only those genetic tests that are sold to laboratories as "test kits" under the Medical Device Amendments of 1976.[16] Tests sold as kits are regulated as "in vitro diagnostic devices," and manufacturers of these kits must submit information to the agency demonstrating that the test is, in FDA parlance, "safe and effective." FDA

[15] 71 Fed. Reg. 22537, 22595 (Apr. 24, 2006).
[16] Pub. L. No. 94-295, 90 Stat. 539 (1976).

reviews the information provided and makes a determination regarding the analytic and clinical validity of the test.

To date, test kits are available for only a handful of genetic tests and the vast majority of genetic tests performed by clinical laboratories do not use test kits. Instead, laboratories for the most part use in-house developed methods (so called "home brew" tests). Even if a kit is available, a laboratory does not have to use it but can decide to offer its own home brew version of the test without the need to undergo FDA review.

FDA has provided mixed signals over time regarding its jurisdiction and willingness to regulate home brew tests. In 1997, the agency asserted that "clinical laboratories that develop such tests are acting as manufacturers of medical devices and are subject to FDA jurisdiction."[17] However, the agency also acknowledged that home brew tests were valuable in "providing novel, highly specialized tests in a relatively short time, sometimes for diseases that affect a relatively small proportion of the population."[18] Thus FDA declined to exercise its jurisdiction because of concerns that unduly stringent regulation of home brew tests could be detrimental to public health. However, in the course of the rulemaking process the agency also stated "at a future date, the agency may reevaluate whether additional controls over the in-house tests developed by such laboratories may be needed to provide an appropriate level of consumer protection. Such controls may be especially relevant as testing for the presence of genes associated with cancer or dementing diseases becomes more widely available."[19]

After a number of years of silence from FDA on the issue of home brew genetic tests, recently the agency has sent a few letters to a small number of companies providing genetic testing services advising them that they might be selling unapproved tests in violation of the law. However, FDA's jurisdiction, or perception of its jurisdiction, remains unclear and the agency has not adopted any systematic regulatory approach with respect to home brew tests.

FDA's lack of clarity with respect to its authority over home brew tests is troubling, and has resulted in a "two path system" for the regulation of genetic tests. Those few companies that have invested the time, money, and effort to develop "test kits" face competition from clinical laboratories using home brews. This uneven regulatory playing field provides a disincentive to the development of test kits with clear evidence of clinical validity before entering the market. While FDA has sent a few warning or "untitled" letters to companies offering particular genetic tests that the agency believes may violate the law, its quixotic enforcement efforts in the absence of a coherent regulatory framework may hinder the availability of valuable genetic tests to the public while failing to address the tests of dubious validity.

Any regulatory system for genetic tests must balance the need for evidence of clinical validity with the desire to foster innovation of new tests. Additionally, such a system

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[17] 62 FR 62243, 62249 (Nov. 21, 1997)
[18] Id.
[19] 61 Fed. Reg. 10484 (Mar. 14, 1996).

must recognize that not all genetic tests raise the same level of concern and therefore must be sufficiently nuanced to take into account the risks, benefits, and foreseeable uses of each particular test. This is no easy task, but is essential if genetic testing is to fulfill its promise of enhancing public health. Unfortunately, at the present time no government entity has been given a clear mandate to oversee genetic tests, thus these fundamental issues are not being addressed. Not for the first time, science has surged forward and public policy simply has not kept pace.

Concerns about Direct-to-Consumer Genetic Testing

Some have argued that direct access to genetic testing is never appropriate, and that a health care provider's intervention is always required. These arguments are premised on the assumption that genetic information is complex, that consumers lack the requisite understanding of genetics to comprehend test results or place them in proper context, and that consumers therefore run the risk of misinterpreting test results and may make bad health care decisions as a result.

While the concerns expressed about this method of delivery for all or some genetic tests could prove to be correct, data are lacking that would provide support either to DTC critics or its supporters regarding whether, in the absence of the intervention of a health care provider, consumers are capable of understanding genetic information and making medically sound decisions.

However, in the context of the current regulatory environment, direct-to-consumer testing may pose real risks to consumers. Absent safeguards to ensure that the laboratories performing tests are competent to do so, that the tests provide clinically relevant information, and that the claims made about tests are accurate and balanced, consumers have no reliable basis to make informed decisions about the benefits and risks of testing. While some DTC companies may be using only high caliber laboratories and offering only tests generally recognized as clinically valid, there is no way for a consumer to distinguish between the decent and the dubious. At best consumers may be wasting their money; at worst they may be foregoing medically appropriate treatment or undertaking medically dubious treatment as a result of testing and the recommendations made by DTC companies based on test results.

The Tip of the Iceberg

While the GAO's investigation of DTC tests focused on a subset of tests known as "nutrigenomic tests," the field of DTC testing is much broader, with test menus that range from the reputable to the reprehensible. Some of the current DTC offerings include tests that purport to predict vulnerability to depression or risk of Alzheimer disease, to detect fetal gender, to determine athletic potential and risk of sports injury, or to identify the cause of infertility or obesity. Like the nutrigenomic tests investigated by GAO, some of these DTC tests are coupled with the sale of products claiming to treat the ailments identified by the tests or to "match" one's genetic profile, such as "customized" supplements to aid in weight loss.

Given the current low regulatory barrier to market entry, the number and types of genetic tests offered directly to consumers can be expected to expand. While some states prohibit laboratories from offering tests or providing test results directly to consumers, many do not. Moreover, given the Internet-based nature of DTC commerce, enforcing state laws against DTC testing is a challenge.

Conclusion

Quality genetic testing requires good tests and competent laboratories. Tests must be offered only when there is sufficient scientific evidence linking a particular genetic variation with a specific health condition or risk. Laboratories reliably must be able to ascertain the presence or absence of a genetic variation and to appropriately communicate results to providers and consumers. Particularly in the case of DTC testing, laboratories must ensure that claims about the meaning of test results are truthful, balanced, and provide appropriate context so that the results are meaningful and useful to consumers.

Without external scrutiny of genetic tests and testing laboratories, physicians and the public have little assurance that the tests they use to make profound medical decisions are reliable and relevant predictors of their disease risk or treatment outcome.

Genetic testing has tremendous potential to improve the health of Americans. If genetic testing is to gain the public's trust and deliver on its promise of improving health, we must have confidence that the laboratories offering these tests are performing them correctly and that the tests themselves yield information that is relevant to health care decision making. That confidence today is unwarranted.

In conclusion, policy action is needed to enhance the analytical and clinical validity of genetic tests. The Genetics and Public Policy Center offers the following recommendations.

1. CMS must issue a proposed regulation to create a genetic testing specialty under CLIA and Congress should hold the agency accountable for timely action.
2. CMS must enforce its existing regulations and ensure that laboratories offering genetic testing are certified and Congress must provide adequate resources to CMS to enable the agency to carry out this vital function.
3. CMS must make a listing of CLIA-certified laboratories and the tests for which they are certified easily accessible to patients, providers, and policy makers.
4. Laboratories should make data on the analytic and clinical validity of the tests they offer publicly available.
5. A fair and balanced system of oversight needs to be created to harmonize inconsistent and incoherent CMS and FDA rules.

Congress took a bold leap in funding the Human Genome Project with the expectation that it would pay off in benefits to human health. That promise can only be realized if we can have confidence in the quality of genetic tests. Congress enacted CLIA and its

amendments with the expectation that it would ensure the accuracy and reliability of clinical laboratory testing, but those expectations have not been met with respect to genetic tests.

The Center applauds the Committee and the GAO for taking this first step in the investigation of questionable practices with respect to genetic tests sold directly to consumers, and urges the Committee to continue to provide leadership in this area so that we can have confidence that genetic tests can be used to improve and not endanger the public's health. Thank you.

The CHAIRMAN. Thank you, Kathy.

It seems to me that the whole thing speaks for itself when GAO submits four samples from one person and gets back four different results. Is that what happened?

Mr. KUTZ. Yes.

The CHAIRMAN. I think the point you are making is between actual and clinical validity. In order to really be valuable, genetic testing has to include environmental understanding of a person's—you know, how they are living, where they are living, what their habits are, all of the factors that go into making up a diagnosis of any kind of genetic impact to a person's health and their propensity to a disease.

Is that basically what you are saying?

Dr. HUDSON. Yes, and in order to document the correlation between a specific genetic mutation or variant and a specific health outcome, it really requires rigorous studies following many people who have the mutation and don't have the mutation, and making a direct correlation between their genes and their health outcomes.

The CHAIRMAN. The clinics have to have valid procedures that are scientifically verifiable, and then it has to be followed up with physicians to take a holistic approach to it or else it really isn't very valid.

Dr. HUDSON. That is right, and there is enormous promise. In the wake of the Human Genome Project, we are trying to unravel the genetic contributions and environmental contributions to common, complex diseases that affect many, many Americans—heart disease, diabetes, and many, many forms of cancer. One of my concerns is that the effort to move genetics into clinical practice and to improve human health is going to be tainted by the ability of bad actors to operate in this area.

The CHAIRMAN. Home kits just are not going to do it. It sounds to me from your opinion, they are simply going to erode credibility in the promise of the genome project and genetics as a part of understanding fully health care and disease.

Dr. HUDSON. If sufficient regulations were in place to assure the analytic validity of tests and the clinical validity of tests, I think then we could really have a conversation about whether it is appropriate for consumers to access some tests directly without a health care provider's intervention.

For example, if there was a test that would tell me which over-the-counter pain medication would be most effective for me, do I really need to go to a physician to get that information? All genetic tests are not created equal, and so we need to have a nuanced approach to whether a health care provider's intervention is required always, sometimes or never.

The CHAIRMAN. We don't have that regulatory structure now?

Dr. HUDSON. We don't have that regulatory structure as a baseline to assure quality today.

The CHAIRMAN. Greg, I wonder if for the record you can identify the companies referred to as websites 1 through 4.

Mr. KUTZ. Sure. Website 1 was Market America and they were marketing via Internet distributor Martin Marketing. Website 2 was Genelex, website 3 was Sciona, and website 4 was Suracell.

The CHAIRMAN. The laboratories?

Mr. KUTZ. The laboratory was Genaissance that processed most of the kits, but also there was SeraCare Laboratories that website number 4 used, we believe, for some of our later tests. Then Genox Corp. processed our urine sample, we believe.

The CHAIRMAN. How about the DNA donors?

Mr. KUTZ. One was a 48-year-old male. He is one of our special agents. The 9-month-old female was my daughter, Katie.

The CHAIRMAN. I understand your investigations also uncovered some difficulties that Sciona encountered when trying to sell these genetic tests in the United Kingdom. Can you share with us what you found?

Mr. KUTZ. Yes. There were consumer groups in the United Kingdom that raised concerns about the validity and the usefulness of similar products being marketed over there. Also they put together a panel of experts similar to the people we consulted with in looking at our 14 fictitious consumers and they concluded that the kits being marketed there were of no value to consumers. The company stopped selling them over there and has come to the United States and is marketing them here.

The CHAIRMAN. So if there are of no value to the British, are they of any value to Americans?

Mr. KUTZ. Well, as I mentioned in my closing, I mean our view is certainly that in a best-case scenario they are of little or no value. Worst-case scenario—and I will use the supplements; $1,200 per year for supplements that you could buy at a grocery store for $35 a year is less than no value. It is a rip-off.

The CHAIRMAN. Did you send your samples directly to labs?

Mr. KUTZ. Some of them were sent directly to labs. Some were sent to the websites who forward them to the labs. So the return envelopes in the kits varied as to where they went.

The CHAIRMAN. I understand that the urine sample that was submitted was a synthetic sample. Did the lab identify it as synthetic?

Mr. KUTZ. It was synthetic urine. It was something called Quick Fix, which is used to beat drug tests, and there is no evidence that the lab identified it as fake urine, basically.

The CHAIRMAN. So they made no conclusion as to it?

Mr. KUTZ. They did make—I mean, it was part of the kit. They tested the cheek swab and the urine.

The CHAIRMAN. So they tested it as urine?

Mr. KUTZ. They tested two, yes. They tested urine and a cheek swab, and then we got the results back. There were no indications that came back to us——

The CHAIRMAN. They did not discern that it was synthetic?

Mr. KUTZ. Not that we can tell, no.

The CHAIRMAN. Are any of the DNA donors—obviously, your daughter is pretty young and I don't know that she would be worried. But the 48-year-old man—is he worried at all about conditions for which they were diagnosed in these tests?

Mr. KUTZ. We are worried about him for other reasons, Senator. [Laughter.]

But for purposes of the tests that were actually made of him, no, I think he knows and we know based on the experts that we have

spoken to that I am not worried about my daughter and I don't think he is worried about the results there.

The CHAIRMAN. It is my understanding that in the course of the investigation the GAO was contacted by a nutritionist after these tests and they tried to sell you the products of this company.

Mr. KUTZ. They tried to sell us on a diet, a nutritional diet that would supposedly help us with the problems that were identified. Within that diet, it was another way to market the supplements. If you actually read through the diet, it looked like some very good dietary suggestions, quite honestly, but within those were also some marketing of specific supplements that, you know, if you take these, according to this, it would help you with whatever gene problems that they identified for you.

The CHAIRMAN. It is my understanding that Sciona has a disclaimer on its website asserting, quote, "its unlimited rights to consumers' information." That, for me, raises a real privacy issue about sensitive data, even if it may be inaccurate data, that is out there in cyberspace.

So I am wondering based on your investigations, what do consumers need to do know about companies' privacy policies and the potential of sending out this kind of information about themselves.

Mr. KUTZ. Well, let's use the example—you just asked me the question about the dietitian who somehow got our results. We don't believe she worked for the company. Somehow, she got the results from one of our fictitious consumers and made a call to us. So it is unclear. I mean, they all made representations, all four websites, that our DNA would be destroyed actually after the results were sent to us and that they would protect all of our other information.

The CHAIRMAN. How would the dietitian have known it?

Mr. KUTZ. Well, we don't know. There is no way to tell exactly whether it was a subcontractor or what other relationship she had to that company.

The CHAIRMAN. But it raises the question that information is out there for anybody to see?

Mr. KUTZ. Yes, that would raise a question.

The CHAIRMAN. In your opinion, what is the most pressing public health threat posed by inadequacies in current oversight in genetic testing?

Mr. KUTZ. Well, I think again there are two parts to this. There is the actual part of the kits and whether or not people should take them, whether they provide value. Certainly, telling someone to stop smoking, to reduce caffeine intake are all great ideas, but you don't really need to buy a kit to actually come up with those.

So I think more significant is the $1,200 and $1,800-a-year supplements that were marketed to us that were linked directly to the results of our genetic tests which said we were at risk of having these very serious medical conditions sometime in the future, and at least implying that if you took these supplements, which again are very, very expensive, this somehow could help you so you would be able to prevent getting these medical conditions.

The CHAIRMAN. So at the end of the day, your ultimate conclusion is that these companies are, in fact, misleading consumers?

Mr. KUTZ. Absolutely, yes.

The CHAIRMAN. No question about it?

Mr. KUTZ. No.

The CHAIRMAN. Senator Talent.

Senator TALENT. Mr. Chairman, I want to thank you for holding this hearing. I am not going to keep this panel too long because I know we have two more coming.

Let me just ask a question that came to mind as soon as the Chairman scheduled this hearing. Why hasn't this industry been better regulated and why has this been allowed to happen? I think Congress passed the underlying legislation in the late 1980's.

Dr. HUDSON. For the regulations of the clinical laboratories and whether or not they can get the right answer reliably over time, the Clinical Laboratory Improvement Amendments are the relevant statute.

Senator TALENT. My understanding is that they give the administrative agencies adequate authority to regulate. Is there a statutory gap here that you see?

Dr. HUDSON. I don't believe that there is necessarily a statutory gap. There is a regulatory gap. Over the years, CMS has created a number of specialty areas for different types of tests—microbiology, toxicology, immunology, et cetera, et cetera, et cetera. When you create those specialty areas, then that comes with certain standards that people who are testing in that area have to meet.

Despite the fact that genetics is arguably one the most rapidly growing areas of diagnostics and has such great promise and is complicated, CMS has failed to create a specialty area for genetics. In 2000, they said they were thinking seriously about it, and now here we are 6 years later and we still don't have a proposed regulation. It is inertia.

Senator TALENT. Does it really make sense to run these tests through mail order? To me, this seems to be a pretty serious area. If properly regulated, do you think this industry serves an important purpose and we can allow this to continue? Or is it just too complicated to do this way?

Dr. HUDSON. I think that there are some genetic tests for complicated, serious medical conditions where a health care provider's intervention is certainly beneficial, if not required. But the notion that all genetic tests are equally complicated and equally serious is probably not the case, and so we need to be a little nuanced about whether or not this is an all-or-none proposition.

We also have a problem with whether or not health care providers are adequately trained and prepared to be able to interpret this information for consumers. Ironically, in regard to the question about privacy, a number of these companies advertise privacy as a selling point. You can do your genetic testing in the privacy of your own home and you don't have to share that information.

But the bottom line is if somebody actually has a mutation that increases their risk for disease or they actually have a disease today, what do we want them to do? We want them to walk directly into their health care provider's office and get medical attention. So the whole notion that this is private is sort of a thin veneer because ultimately that information will be in the medical record and protected by HIPAA and other laws.

Senator TALENT. If adults are aware of what they are receiving and still decide they would like to purchase for whatever reason.

I will not prevent anyone from doing so. But it seems to me that to the extent this has real medical value in identifying people who are at high risk, you would think that the profession would have begun to incorporate it into some regular testing or they would recommend it for certain people who have other characteristics that might make them high-risk.

Do you understand what I am saying?

Dr. HUDSON. Yes, yes, absolutely.

Senator TALENT. Well, much of this refers to what the other two panels are going to testify to, Mr. Chairman. I appreciate your holding this hearing. Thank you.

The CHAIRMAN. Thank you, Senator Talent.

A couple of follow-ups. Mr. Kutz, one of the companies in your report, Suracell, has represented to this Committee that they do not conduct direct sales to consumers. When pressed on the point about sales from Suracell's website, they modified their response and indicated that when consumers purchase test kits from Suracell's website, they are assigned a physician in their area based on their zip code. When asked point-blank if a consumer can purchase a test kit without the involvement of a physician, Suracell's response was no. I note in their written statement to the Committee, Suracell has further modified its response and acknowledged that 28 percent of its sales are direct to consumers.

Mr. Kutz, my question to you is with respect to the tests that GAO purchased from Suracell, how many kits did you purchase and for how many of those tests did you have to go through a doctor's office to obtain either the test kits or test results?

Mr. KUTZ. We purchased three and there were no doctors involved in consulting with us at any stage that we were aware of, at least. If they were assigned to our three cases, they never contacted us.

The CHAIRMAN. You weren't aware of it?

Mr. KUTZ. No.

The CHAIRMAN. Until this morning—and I say this morning because Sciona has just changed its website—Sciona advertised that its lab, which we know to be Genaissance, is CLA-certified. I presume that to mean CLIA, or C–L–I–A. Your investigation reveals some interesting facts about Genaissance CLIA certification as it pertains to nutrigenetic tests.

Could you please tell the Committee what your investigation revealed?

Mr. KUTZ. I am not sure we know exactly what their CLIA certification is. We did not challenge that they were CLIA-certified. The actual lab that did the urine tests had represented to us that they were not CLIA-certified. So I don't believe that Sciona had represented that they were not CLIA-certified. They may not be CLIA-certified for the specific tests that we did and that may be the issue you are talking about.

The CHAIRMAN. Are you aware that Genaissance refused CLIA recertification inspection for these very tests?

Mr. KUTZ. I was aware of that, yes.

The CHAIRMAN. It probably indicates they are not certified.

Thank you both very much. We appreciate your work and your expertise in helping this Committee to understand this very real issue of consumer, buyer beware.

We will now call up our second panel. On our second panel, we have representatives from several of the companies referenced in today's GAO testimony. Ms. Rosalynn Gill-Garrison is the chief science officer for Sciona. Dr. Carol Reed is senior vice president and chief medical officer for Genaissance Pharmaceuticals. Mr. Kristopher King is the CEO of Suracell. Dr. Ramarathnam is president of Genex Corporation. Mr. Howard Coleman is CEO of Genelex Corporation.

If you will each stand and raise your right hand, do you promise that the testimony you are about to give will be the truth, the whole truth and nothing but the truth, so help you God?

Individually. Rosalynn?

Ms. GILL-GARRISON. I do.

Dr. REED. I do.

Mr. KING. I do.

Mr. RAMARATHNAM. I do.

Mr. COLEMAN. I do.

The CHAIRMAN. Thank you very much.

Rosalynn Gill-Garrison, we will start with you.

STATEMENT OF ROSALYNN GILL-GARRISON, CHIEF SCIENCE OFFICER, SCIONA, BOULDER, CO

Ms. GILL-GARRISON. Thank you. I would like to thank the Committee and Senator Smith for the opportunity to appear before you today. My name is Rosalynn Gill-Garrison and I am the chief science officer for Sciona, Inc. Sciona was formed with the goal of bringing the benefits of the Human Genome Project directly to the consumer. The initial meeting that led to the formation of our company was actually held on the day that President Bill Clinton and British Prime Minister Tony Blair announced that the first draft of the Human Genome Project was now complete.

At this initial meeting, the cornerstones of the philosophy of Sciona were laid down that the knowledge resulting from this enormous public and private investment should be used to benefit the average person on the street and that each member of the public should be able to learn directly about his or her own genetic information. The goal of our company is to use this information to provide health care information which is focused on health and wellness rather than the treatment of illness, and it is the duty of our company to deliver this information in an ethical and responsible manner.

Sciona decided to focus on the growing body of knowledge of the impact of genetic variation on response to dietary and environmental factors. This was a deliberate decision to focus on health- and wellness-based applications and to focus in an area in which there was a significant body of research that substantiated the links between dietary and environmental factors and genetics.

Sciona's nutritional advisory report which we have actually provided for participants in this conference includes information on 19 genes, 24 variations in these genes, and 18 particular nutritional and lifestyle factors. The report has been written in language that

is intended to be easily understood by the consumer. However, technical information such as the exact genetic variation has been included so that individuals or health care practitioners can refer directly to this genetic information, if required.

The report describes how the interaction of these genes and nutritional factors can play a role in different areas of health. Sciona does not sell any products in conjunction with this report. These reports do not diagnose any disease, but are focused on nutritional and lifestyle status to promote general health and wellness.

The Sciona nutritional lifestyle information service has been developed through an extensive survey of peer-reviewed literature from the fields of nutrition research, biochemistry, epidemiology and molecular biology. In order to build further upon the knowledge available in the public domain, Sciona has actually invested in collaborative research with academic groups interested in exploring gene-diet and gene-environmental relationships.

The laboratory work for Sciona is outsourced and the company maintains close scrutiny on the results and performance of the laboratory testing supplier, which is Clinical Data, Inc. Each batch of samples which are run by the supplier includes a set of blinded controls supplied by Sciona for processing. The laboratory is not aware of the nature of the blinded samples, and so when the results are supplied back to Sciona, these blinded controls are used as a measure of reproducability and reliability of the laboratory results. Pass/fail criteria have been set in which both Clinical Data internal controls and Sciona blinded controls must be in concordance before any set of results is released for report production.

So in conclusion, Sciona is safely, effectively and ethically providing important genetic information to consumers concerning their nutritional well-being, contributing to their health and wellness. Sciona is not involved in diagnostic or disease-related services or information. Sciona believes that the nutritional genetic information provided can best assist consumers if it is available to the consumer through direct access to the service, and we look forward to the development of a regulatory environment and we intend to fully comply and cooperate with the regulatory authorities.

Thank you.

[The prepared statement of Ms. Gill-Garrison follows:]

Sciona

Rosalynn Gill-Garrison
July 20, 2006

I.Company Background

Sciona was formed in the United Kingdom in the summer of 2000 with the goal of bringing the benefits of the Human Genome Project directly to the consumer. The initial meeting that led to the formation of our company was held on June 26, 2000, coincidentally, the day that former president Bill Clinton and British Prime Minister Tony Blair announced that the first draft of the human genome was now complete. At this initial meeting, the cornerstones of the philosophy of Sciona were laid down:

- **The knowledge resulting from the enormous public and private investment should be used to benefit the average person on the street**
- **Each member of the public should be able to learn directly about his or her own genetic information**
- **The goal of the company is to use the information to provide health care information focused on health and wellness, rather than treatment of illness**
- **It is the duty of the company to deliver this information in an ethical and responsible manner**

Sciona decided to focus on the growing body of knowledge of the impact of genetic variation on response to dietary and environmental factors. This was a deliberate decision to focus on health and wellness based applications, and to focus in an area in which there was a significant body of research that substantiated the links between dietary and environmental factors and genetics. Our goal in founding the company was to use the power of genetic information to help people maintain their health, a fundamental change from disease management based health care.

The founders of Sciona believed that delivering information directly to the consumer was an essential step in helping to drive this change toward using genetics to support health and wellness. Sciona became the first company in the world to provide this type of genetic information and advice, and so as the pioneers in this field, we felt a duty of care to provide a service that was credible,

scientifically-based, ethical, and which maintained the highest standards of privacy protection. The founders of Sciona worked to make every aspect of the business meet best practice, with the goal of establishing standards for what is now a rapidly growing industry, to ensure protection of the individual consumer.

To ensure that our company conformed to the highest standards, we engaged the services of top leaders in the field:

- Ethics – before the first product of Sciona was developed, we worked extensively with a highly respected Ethics consultant from the Ethox group in Oxford, United Kingdom. This consultant reviewed the first products that were developed by Sciona, and provided invaluable feedback on the language that was used, and how the information was communicated. Sciona funded a PhD project to examine the ethical and societal implications of genetic testing. Sciona also participated in an extensive review of emerging biotechnology companies with a focus on ethics, entitled Bioindustry Ethics by D. Finegold, C. Bensimon, A. Daar and others, published by Elsevier in 2005. We have subsequently used consultants based in North America, and have recently completed the formation of a formal Ethics Advisory Board. Sciona has been highlighted as a company that has established ethics as the necessary foundation for any company in genomics in recent press articles.

- Privacy Protection – the original founding team of Sciona included experts in computer software and internet security, so we were able to build an infrastructure that provided the highest degree of protection for the safeguarding of each individual's personal and genetic information.

- Scientific Review – Sciona has a Science and Business Advisory Board, with leading experts in the fields of gene-diet interactions, also referred to as nutrigenomics and/or nutrigenetics, as well as industry leaders in health care and food industry. The board has reviewed our products, our publications, and our research and development projects extensively.

II. Sciona's Products and Services

Sciona offers a nutritional lifestyle information service directly to the consumer. Sciona does not manufacture, produce or sell dietary supplements or any other food-related products, nor does the company obtain any revenue from sales of products from any of our commercial partners. Our business activities are solely based on the provision of nutritional lifestyle information. Our information service consists of the following:

1. The consumer purchases a kit, containing cheek cell collection swabs, a Lifestyle Questionnaire, and a return mailer envelope, through a variety of distribution channels, including health care practitioners, internet, direct sales agents, and pharmacies.
2. The kit is designed for the consumer to use in the privacy of his or her own home. The individual uses the cheek swabs to collect cells from the inside of his cheek, then fills out the Lifestyle Questionnaire, and returns the swabs and questionnaire to Sciona. The questionnaire includes a consent form, which must be signed by the individual before the samples can be processed. Also note that individuals must have reached the legal age of consent in the country of origin, usually 18 years of age, for the sample to be processed. Sciona does not process samples from children.
3. Samples are received by Sciona, and the personal data from the questionnaire is recorded as well as the bar codes on the sample tubes containing the cheek swabs and on the questionnaire.
4. The sample tubes which have no personal identifying information on them, simply a bar code, are then delivered to the independent laboratory which carries out the genetic analysis for Sciona on a contract basis.
5. The questionnaire is scanned by Sciona. The questionnaire output is put into an electronic file, which is merged with the electronic data output from the laboratory. These two data sets are matched by the bar codes. The information is then delivered via secure electronic means to Sciona's proprietary Rules Engine, which produces a report for each individual. The report is delivered either directly to the individual or to the individual's health care practitioner, if the individual has so requested by signed consent.

Sciona Report

Sciona's nutritional advisory report in its current product configuration includes information on 19 genes, 24 variations in these genes and 18 particular nutritional and lifestyle factors. The report has been written in language that is intended to be easily understood by the consumer; however, technical information such as the exact genetic variation has been included so that individuals or health care practitioners can refer directly to the genetic information if required. The report describes how the interaction of these genes and nutritional factors can play a role in different areas of health; including heart

health, bone health, antioxidant and detoxification function, inflammation, and insulin sensitivity. Many of the 19 genes have an impact on more than one of these health areas, so this information is also shared with the consumer.

Each of the 19 genes selected for the current product has a clear gene-diet or gene-environmental relationship that has been demonstrated in peer-reviewed scientific publications. Gene-environmental relationships may include physical activity, body mass index, or tobacco smoking. Each gene may play a role in more than one of the areas of focus for Sciona's nutritional advisory report.

Each of the 5 health areas that is covered by the current report includes the following elements:

- Table with genes and variations identified
- Action map graphic element combining genetic profile with nutritional analysis
- Bar graphs in which the individual's current estimated nutritional intake is measured against a goal intake of nutrients

Finally, the report contains a section with additional tips and advice on where to find rich sources of particular nutrients and how best to prepare foods to maximize the nutrient value of these foods. Sciona does not sell any products in connection with the report.

Looking into more detail on the health areas covered and the nutritional and environmental relationships, the report consists of information on the following areas:

Heart Health: This section of the report focuses on 14 variants of 13 genes, which have a role in the following:

- Lipid metabolism - responsive to saturated fats and cholesterol in the diet
- B-vitamin metabolism and homocysteine remethylation - responsive to levels of B vitamins in the diet
- Antioxidant function and inflammation - responsive to levels of antioxidants, omega 3 fatty acids, tobacco smoking, and physical activity
- Vascular tone - responsive to physical exercise, omega 3 fatty acids and smoking

Bone Health: This section of the report focuses on 7 variants of 4 genes, which have a role in the following:

- Calcium and Vitamin D absorption - responsive to dietary calcium and dietary vitamin D plus exposure to sunlight, smoking and caffeine consumption
- Bone structure and remodelling - responsive to omega 3 fatty acids

- Overall bone integrity - responsive to Body Mass Index (BMI) and physical exercise

Antioxidants and Detoxification: This section of the report focuses on 7 variants of 6 genes, which have a role in the following:

- Phase II detoxification - responsive to dietary allium and cruciferous vegetables
- Antioxidant function - responsive to levels of antioxidants in the diet and tobacco smoking
- Nitric oxide generation - responsive to omega 3 fatty acids and smoking

Inflammation: This section of the report focuses on 7 variants of 6 genes, which have a role in the following:

- Pro-inflammatory cytokine production - responsive to omega 3 fatty acids
- Antioxidant function and phase II detoxification - Responsive to levels of antioxidants in the diet, dietary allium & cruciferous vegetables and smoking
- Overall inflammatory profile - responsive to BMI

Insulin sensitivity: This section of the report focuses on 6 variants of 5 genes, which have a role in the following:

- Levels of insulin secretion and glucose release into the blood stream - responsive to dietary glycemic load
- Glucose and lipid metabolism - responsive to dietary glycemic load and ratio of unsaturated to saturated fatty acids in the diet
- Sensitivity of cells to insulin - responsive to dietary omega 3 fatty acids
- Vascular flow - responsive to physical exercise and BMI

These reports do not diagnose any disease but are focused on nutritional and lifestyle status to promote general health and wellness.

Sciona Rules Engine

Each report that an individual receives from Sciona is generated by a proprietary software system developed by the Research & Development Team at Sciona, in collaboration with a bespoke software development company, Solcom, Ltd. The software consists of a series of algorithms in which genetic variations are scored according to their biological impact and the resulting genetic score is put together with nutritional analysis from the Lifestyle Questionnaire provided by each consumer. Then the Rules Engine provides the integrated information in the form of visual feedback, as well as instructional language to help the consumer make nutritional and lifestyle choices. The software architecture is a Microsoft SQL relational database, into which genetic and other data for each individual is delivered by secure electronic methods. The output of the rules engine is a

locked pdf file which cannot be altered electronically, together with CSV (comma separated variable) files and log files which are used for quality control purposes and customer tracking information. Reports are delivered to a secure printer for production, and the electronic files are encrypted and stored on physical medium, with multiple layers of encryption to ensure maximum security of information. The rules engine is currently being validated to GAMP4 standards (Good automated manufacturing practice, a quality standard for software functionality), with completion expected in approximately 3 months time.

Scientific background

The Sciona nutritional lifestyle information service has been developed through an extensive survey of peer-reviewed literature from the fields of nutrition research, biochemistry, epidemiology and molecular biology, and the genes which have been selected have had to meet our internal selection criteria:

a. The gene-diet or gene-environmental relationship must have appeared in multiple reports in credible, peer-reviewed journal articles.
b. The genetic variation cannot be a rare form found in less than 1% of the population
c. There must be some nutritional or environmental factor which has been shown to have an impact on the effect of the genetic variation

In order to build upon the knowledge available in the public domain, Sciona has invested in collaborative research with academic groups interested in exploring gene-diet and gene-environmental relationships.

Research collaborations:

University of Southampton, UK:

The influence of genes on the ability of Vitamin E supplements to reduce inflammation in healthy people and patients with rheumatoid arthritis.

University of Reading, UK:

Study 1: Examine the impact of genotype on fasting and postprandial lipid metabolism and vascular function and on responsiveness to fish oil fatty acids in pre- and post- menopausal women.

Study 2: Examine the impact of fasting and postprandial lipid metabolism in both men and women.

Micro2DNA:

Integrated polymer-based micro fluidic micro system for DNA extraction, amplification, and silicon-based detection for point of care genetic testing

and information use by health care practitioners. EU/FP6 - Specific Targeted Research Projects (STREP)

University of London School of Pharmacy:
PhD project to examine ethical and regulatory implications of genetic testing.

University of Portsmouth:
Genetic predisposition to cytokine-mediated fatigue in ultra-endurance athletes and chronic fatigue syndrome patients

III. Sales and Distribution of Sciona's Products

Sciona's nutritional advisory service is sold and marketed through a variety of distribution partners:

1. Health Care Practitioners
2. Pharmacies
3. Direct Marketing Organizations
4. Internet Distribution

Through its distribution channels, Sciona sells kits containing the cheek cell collection swabs and questionnaire, Sciona orchestrates the processing of the samples, and produces the personalized advisory kits.

IV. Quality

The laboratory work for Sciona is outsourced, and the company maintains close scrutiny on the results and performance of the laboratory testing supplier. Each batch of samples which are run by the supplier includes a set of blinded controls supplied by Sciona for processing. The supplier is not aware of the nature of the blinded samples, and so when the results are supplied back to Sciona, these blinded controls are used as a measure of reproducibility and reliability of the laboratory results. The laboratory supplier also uses internal controls chosen by the supplier, and pass/fail criteria have been set in which both internal supplier controls and Sciona blinded controls must be in concordance before any set of results is cleared for report production.

V. Conclusion

Sciona is safely, effectively and ethically providing important genetic information to consumers concerning their nutritional well-being, contributing to their health and wellness. Sciona is not involved in diagnostic or disease-related services or information. Sciona believes that the nutritional genetic information provided can best assist consumers if it is available to the consumer through direct access to the service.

The CHAIRMAN. Thank you, Rosalynn.
Dr. Reed.

STATEMENT OF CAROL R. REED, M.D., SENIOR VICE PRESIDENT AND CHIEF MEDICAL OFFICER, CLINICAL DATA, INC

Dr. REED. First of all, thank you very much, Senator Smith, for the opportunity to appear here today. As you know, my name is Carol Reed. I am chief medical officer of Clinical Data, Inc. We are a company that has been in the forefront of the development of pharmacogenetics research and testing for many years. We provide pharmacogenomic and molecular services to the research industry, including clinical trial aspects of drug development, but key to our business is our ability to discover, develop and commercialize genetic tests to guide drug development and utilization.

As the Committee is well aware, drug spend is one of the largest components driving the total cost of health care, despite many efforts to contain it. Health care providers and payers face the difficult task of deciding which drugs to be prescribed to specific patients and are suitable for reimbursement. These decisions are based on medical outcome studies and economic benefit factors, but with little knowledge of which individual patients are most likely to benefit from a specific drug.

In fact, managed care plans employed by payers and prescription benefit managers have a significant impact on providers' decisions as to which drugs should be prescribed. All participants in the decision to prescribe would benefit from the ability to more clearly identify drugs that are most efficacious and safest for a specific individual or patient population.

The medical community generally acknowledges that most drugs work more effectively for some patients than for others. The genomic blueprint each person inherits from his or her biological parents is contained within a person's DNA and determines not only the obvious physical characteristics that differentiate us, such as height, hair color and eye color, but also has a large impact on how we respond to medications. By understanding genetic variation and its relationship to drug response, it is possible to determine which individuals are most likely to benefit from a given drug even before the drug is prescribed.

Clinical Data's main focus is the development and delivery of genetic tests that may be used to more confidently predict an individual's response to an intervention. As an example, our FAMILION test is used to identify mutations in ion channel genes that are associated with Familial Long QT Syndrome. This test has had a very direct and positive impact on patients' lives, helping physicians determine the right intervention for each patient, as well as assisting the family in ascertaining the status of their relatives, as these syndromes may be asymptomatic until presenting suddenly with syncope, seizures or death.

This test requires a provider's order, is performed in our CLIA-certified and compliant laboratory in New Haven, and test results are reported directly to the provider for use in decisionmaking as clinically indicated. Despite the absence of an approved proficiency testing program for this high-complexity test, we conduct proficiency testing with the assistance of academic experts. This is the

model that Clinical Data intends to follow as we develop and deliver pharmacogenetic tests to payers and providers.

Regarding nutrigenomic testing, in 2002 Genaissance Pharmaceuticals entered into an agreement with Sciona, a nutrigenomics testing company. In the good-faith opinion of the company at that time, this testing did not fall under CLIA oversight. The Genaissance laboratory accepts de-identified samples from Sciona customers, extracts DNA and performs genotyping. We have a quality control process in place that meets CLIA standards for proficiency testing and our accuracy in genotypes calls is over 99 percent. The genotying results are sent to Sciona, who provides interpretation and a report to their customers.

Genaissance Pharmaceuticals was acquired by Clinical Data in October 2005. Clinical Data is supportive of the interest on the part of CMS and CLIA and the Federal Government to consider increasing regulatory oversight of this testing, and the Committee may well be aware that we have now undergone CLIA auditing of our nutrigenomics testing and we are now awaiting the results of that audit.

The CHAIRMAN. But did you actually refuse their reauthorization?

Dr. REED. At the time when we were conducting the test earlier and felt that it was not under CLIA regulation, yes, we did refuse that inspection, but we have since permitted that inspection.

The CHAIRMAN. You refused it, but you have since allowed it?

Dr. REED. Correct.

The CHAIRMAN. You are awaiting the results for that?

Dr. REED. Correct.

The CHAIRMAN. I guess my problem was just that that fact, coupled with GAO's finding of inconsistent test results, have clearly led to some concern on the part of the Committee.

Dr. REED. Understandable.

The CHAIRMAN. You understand, OK. Thank you very much, Carol.

Dr. REED. You are welcome.

[The prepared statement of Dr. Reed follows:]

July 27, 2006

Opening Statement Presented to the United States Senate, Special Committee on Aging, by Carol R. Reed, MD, Senior Vice President, and Chief Medical Officer, Clinical Data, Inc.

My name is Carol Reed and I am Chief Medical Officer of Clinical Data, Inc. I would like to thank the Committee and Senator Smith for the opportunity to appear before you today. Clinical Data is a company that has been in the forefront of the development of pharmacogenetics research and testing for many years. We provide pharmacogenomic and molecular services to the research industry, including clinical trial aspects of drug development, but key to our business is our ability to discover, develop, and commercialize genetic tests to guide drug development and utilization. As the committee is well aware, drug spend is one of the largest components driving the total cost of healthcare, despite many efforts to contain it. Healthcare providers and payers face the difficult task of deciding which drugs should be prescribed to specific patients and are suitable for reimbursement. These decisions are based on medical outcome studies and economic benefit factors but with little knowledge of which individual patients are most likely to benefit from a specific drug. In fact, managed care plans employed by payers and Prescription Benefit Managers have a significant impact on providers' decisions as to which drugs should be prescribed for a specific patient. All participants in the decision to prescribe would benefit from the ability to more clearly identify drugs that are most efficacious and safest for a specific individual or patient population, resulting in optimized patient care and outcomes.

The medical community generally acknowledges that most drugs work more effectively for some patients than for others. The genomic blueprint each person inherits from his or her biological parents is contained within a person's DNA and determines not only the obvious physical characteristics that differentiate us, such as height, hair color and eye color, but also has a large impact on how we respond to medications. By understanding genetic variation and its relationship to drug response, it is possible to determine which individuals are most likely to benefit from a given drug, even before the drug is prescribed.

Clinical Data's main focus is the development and delivery of genetic tests that may be used to more confidently predict an individual's response to an intervention. As an example, our FAMILION test is used to identify mutations in ion channel genes that are associated with Familial Long QT Syndrome and other inherited arrhythmogenic disorders. This test has had a very direct and positive impact on patients' lives, helping physicians determine the right intervention for each patient, as well as assisting the family in ascertaining the status of their relatives, as these syndromes may be asymptomatic until presenting suddenly with syncope, seizures, or death. This test requires a provider's order, is performed in our CLIA-certified and compliant laboratory in New Haven, CT, and test results are reported directly to the provider for use in decision-making as clinically indicated. Despite the absence of an approved proficiency testing program for this high-complexity test, we conduct proficiency testing with the assistance of academic experts. This is the model that Clinical Data intends to follow as we develop and deliver pharmacogenetic tests to payers and providers.

Regarding nutrigenomic testing: in 2002, Genaissance Pharmaceuticals entered into an agreement with Sciona, a nutrigenomics testing company. In the good faith opinion of the company at that time, this testing did not fall under CLIA oversight. The Genaissance laboratory accepts samples from Sciona customers, extracts DNA, and performs genotyping. The genotyping results are sent to Sciona who provides interpretation and a report to their customers. Genaissance Pharmaceuticals was acquired by Clinical Data, Inc., in October 2005. Clinical Data is supportive of the interest on the part of CMS/CLIA and the federal government to consider increasing regulatory oversight of this testing.

I would again like to thank the committee for the opportunity to provide input and assistance as the Committee navigates this challenging and exciting new terrain. We support efforts to assure that all genetic testing meets standards for both process and analytical and clinical utility and stand ready to assist Congress as it explores these issues.

Sincerely,

Carol R. Reed, MD, FACP, FACC

The CHAIRMAN. Kristopher King.

STATEMENT OF KRISTOPHER KING, CHIEF EXECUTIVE OFFICER, SURACELL, INC., MONTCLAIR, NJ

Mr. KING. Mr. Chairman and members of the Committee, my name is Kristopher King and I am the chief executive officer of Suracell, Inc. We are sorry that our chief science officer, Dr. Vincent Giampapa, was unavailable to testify today.

I would like to begin by stating some key points about Suracell. Suracell is not a laboratory and does not perform genetic testing, but recommends it as one component of the program we offer to our clients. Suracell offers nutritional advice and supplements to our clients. Suracell does not make any diagnosis in relation to disease, medical conditions or prescription drugs. Suracell has a robust privacy policy and Suracell has a comprehensive informed consent process. Suracell's program is based on sound and accepted scientific research, and Suracell is committed to the ongoing education of an informed client base.

Suracell was incorporated in 2004 with the mission of providing consumers with state-of-the-art, personalized nutritional information and products that can help optimize wellness. Suracell's chief science officer is Vincent Giampapa, and based on his 10 years of practicing age management medicine, Dr. Giampapa observed that within specific types of DNA and biomarker testing and focused nutritional advice, his patients' overall health status in several areas greatly improved in a relatively short period of time. This research was published. Suracell is guided by an advisory board comprised of specialists in genetics, microbiology, gerontology and several M.D.s.

One of the three components of Suracell's personalized nutritional program is an analysis based on information obtained from the results of a buccal cell-based gene variant test that identifies 26 gene variants that are associated with the efficiency of five metabolic processes—glycation, inflammation, methylation, oxidative stress and DNA repair. One example would be for a consumer whose profile reveals a deficient value for the SNP MTHFR which relates to homocysteine levels. This consumer would benefit from increasing their intake of folic acid.

The correlation between particular genetic variations and optimal nutritional support are based on peer-reviewed scientific literature. Suracell offers a DNA test and the laboratory that processes this test is SeraCare BioServices, based in Maryland. SeraCare uses a home brew method for processing DNA samples submitted as part of Suracell's nutritional program. Suracell understands from SeraCare that its lab has CLIA certification. SeraCare destroys specimens upon completion, so those samples cannot be used for any other purpose.

Suracell provides clients and their health care professionals with the results of the analysis provided by our program and recommends nutritional supplements based on those results. The Suracell program is designed for informed clients between the ages of 40 to 60 because the processes affecting glycation, inflammation, methylation, oxidative stress and DNA repair are typically less efficient at this age due to genetic inheritance, environmental expo-

sures and lifestyle. But research indicates that improvements can still be made within this age range to enhance overall wellness.

The vast majority, approximately 85 percent, of Suracell's customers are in the 40 to 55 age range. Suracell does not sell to anyone under the age of 18 and requires each customer to provide informed consent. Suracell's consent process requires that customers actively consent to the testing of the samples they provide in advance of any testing procedures and, separately, that they consent to have their physician or health care practitioner receive the results of the analysis of such tests.

Suracell has a detailed published privacy policy available on our website. Suracell adheres to FTC standards for privacy and protection of consumer information. In addition, Suracell maintains compliance with the privacy and information provisions of HIPAA.

You asked us to address direct-to-consumer genetic testing. The most important aspect of this is the accuracy of the testing and the results provided. In some cases, consumers may be making life-altering decisions based on the results of these tests, particularly in the area of paternity, disease screening and prenatal screening. An expansion of the CLIA standard to include the sub-specialty of genetic testing would be a useful step in this process.

You asked us for our views on the article "Federal Neglect: Regulation of Genetic Testing," in "Issues in Science and Technology," Spring 2006. Suracell agrees with the following points raised by the article. There should be a specific CLIA standard for the subspecialty of genetic testing. There needs to be government oversight of the accuracy of tests. Suracell agrees with FTC oversight of advertising claims made by companies offering direct-to-consumer DNA testing.

Suracell strongly believes that consumers who choose to do so can benefit from knowing their genetic variance as it relates to the aforementioned metabolic processes because such knowledge enables them to make dietary and behavioral changes to improve their overall wellness. In addition, Suracell believes that in order for the benefits of new genetic knowledge and technology to be realized, the public must be assured that genetic testing is accurate.

Suracell again recommends that establishing genetic testing specialty certification within CLIA may be an effective strategy to achieving oversight of genetic testing and is supportive of this action.

Thank you.

The CHAIRMAN. Mr. King, you are testifying on behalf of Dr. Giampapa?

Mr. KING. I am testifying on behalf of Suracell.

The CHAIRMAN. Suracell.

Mr. KING. Dr. Giampapa, our chief science officer, would be better at explaining the science behind the program.

The CHAIRMAN. Well, he is your chief science officer?

Mr. KING. Yes, sir.

The CHAIRMAN. It is my understanding he is a plastic surgeon.

Mr. KING. Yes, sir.

The CHAIRMAN. How does that qualify him to do genetic testing?

Mr. KING. Well, over a 10-year period, Dr. Giampapa has believed that plastic surgery focusing on the outside of the body is

really deficient and doesn't focus on the total body. For over 10 years, he has worked on looking at inside-out approaches to improve wellness.

The CHAIRMAN. But my point is just simply that if he is your chief science officer and he is a plastic surgeon working in the very technical field of genetics, I guess it raises a question.

Mr. KING. Well, we do have an advisory board. We have several geneticists, molecular biologists that work on a full-time or a part-time basis advising the company.

The CHAIRMAN. You would admit, though, genetics is a much more complicated field than plastic surgery?

Mr. KING. Yes.

The CHAIRMAN. You have indicated that SeraCare is CLIA-certified, but you also use Genox as a laboratory and have represented to the Committee staff that you verified Genox' CLIA certification. We know that Genox is not CLIA-certified. Can you address the misrepresentation?

Mr. KING. Well, there are three components to our program. We have the genetic test which is done by SeraCare. We have the assessment which is done by Genox, and we have the lifestyle questionnaire. I was unaware of the lack of CLIA certification in the Genox laboratory.

The CHAIRMAN. So it was ignorance on your part?

Mr. KING. Yes, sir.

The CHAIRMAN. You didn't know they weren't certified?

Mr. KING. Yes, sir.

The CHAIRMAN. But it was represented to us by you that they were.

Mr. KING. I honestly don't recall when I spoke with the GAO if I had made that claim. If you say I have, then I, you know——

The CHAIRMAN. Well, it simply goes to this whole credibility issue which leads to this hearing today. I am not trying to cast aspersions on you personally, or any of you.

Mr. KING. I understand.

The CHAIRMAN. But we have a responsibility to consumers and this is just so loosy-goosy here that I am really concerned about what you are selling, what it means, the doom and gloom, the validity, the premium price that is being charged, the peddling of health advice, frankly, when there isn't the basis for it.

I am worried that we are exploiting and misleading people—this industry. I am very alarmed that consumers are being preyed upon, that this great promise of the Genome Project is being exploited in a way that is victimizing people who have no assurance of the accuracy, validity or utility of these tests.

I want to emphasize, too—and we are going to get to this—privacy and confidentiality. Who do you share it with? Why does a nutritionist follow up with the GAO investigating, wanting to sell them something based on something from a genetic home brew kit?

[The prepared statement of Mr. King follows:]

SURACELL

STATEMENT OF KRISTOPHER KING, CHIEF EXECUTIVE OFFICER, SURACELL, INC. BEFORE THE SPECIAL COMMITTEE ON AGING, UNITED STATES SENATE

"Direct To Consumer Genetic (DNA) Testing"

July 27, 2006

SURACELL

Introduction

Mr. Chairman and Members of the Committee, my name is Kristopher King, and I am the Chief Executive Officer of Suracell Inc.(biography attached). Suracell is looking forward to helping provide clarity and substance to questions related to direct to consumer genetic testing. We welcome the opportunity to provide the committee with Suracell's business approach, and the steps we have taken on behalf of our clients in the area of consumer protection.

Our original response to the Committee, that we respectfully decline to appear, was based purely on the fact that we are a small company and we felt that the unavailability of our Chief Science Officer, Dr. Vincent Giampapa, on such short notice would make our response inadequate.

I have been asked to provide the Committee with a response that is as comprehensive as possible under these circumstances, that addresses the concerns and interest of the Committee, as they have been conveyed to me by the Chairman's staff.

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Introduction to Suracell, Inc.

There are seven key points that should be noted with regard to Suracell:

1. Suracell does not perform genetic (DNA) testing.
2. Suracell offers nutritional advice and supplements to our clients.
3. Suracell does not make any recommendations or diagnoses in relation to disease, medical conditions or prescription drugs.
4. Suracell has a privacy policy carefully designed and implemented to protect the privacy of client information.
5. Suracell's program has a comprehensive informed consent process.
6. Suracell's program is based on sound and accepted scientific research.
7. Suracell is committed to the ongoing education of an informed client base.

Suracell was incorporated in 2004 with the mission of providing consumers with state of the art **personalized nutritional information and products** that can help optimize wellness. Suracell's Chief Science Officer is Vincent C. Giampapa, MD, FACS, whose biography can be found on Suracell's website at http://www.suracell.com/about_us/giampapa.asp .

Based on his ten years of practicing age management medicine, Dr. Giampapa observed that with specific types of DNA and biomarker testing, and focused nutritional advice, including specific nutritional supplements, his patients' overall health status in several areas greatly improved in a relatively short period of time, and this improvement could be

measured by follow-up testing.

This research was published, and further advances in the field of nutrigenomics confirmed this research, which led to the company's inception.

Suracell is further guided by a **scientific advisory board** comprised of specialists in genetics, microbiology, gerontology, and several MDs.

Suracell's Program

Suracell does not perform DNA testing.

Suracell's program is not designed or intended to diagnose any disease, medical or genetic condition, or recommend any treatment for any disease, medical or genetic condition.

Suracell's program has no involvement, coverage or reimbursement of any kind from either health insurance carriers, Medicare, Medicaid or any other program.

Aging is a complex and multifactorial process that includes reduced cell replication, impaired cell maintenance and impaired cellular repair.

Current medical practice places great emphasis on the use of prescription drugs for

disease prevention or control because they are an easy alternative to implementing changes in diet and lifestyle. Studies have clearly shown that lifestyle and diet changes have not only psychological and economic benefits but are also important in disease prevention and longevity.

Suracell's program is designed and intended to provide clients with information enabling them to optimize their general wellness, via supplements, diet and lifestyle changes.

Suracell provides a service to consumers enabling them to receive nutritional advice and a supplement regimen that is personalized to their needs. For example, millions of consumers visit retail locations that sell vitamins and supplements and purchase various products without any real knowledge of which of those products are appropriate for them. Suracell's program brings efficiency to the process by recommending any needed supplementation at a personal level, which then means that a consumer may not take unnecessary supplements.

One of the three components of Suracell's personalized nutritional program is an analysis based on information obtained from the results of a **buccal cell based gene variant test** that identifies **twenty-six** gene variants that are associated with the efficiency of five metabolic processes: glycation, inflammation, methylation, oxidative stress and DNA repair.

The results of the analysis can help educate a client about the type of nutritional support that may benefit them. For example, a consumer whose profile reveals a deficient value for gene SNP (variant) LEPR K109R, which relates to the regulation of insulin and blood sugar, may benefit from including supplements containing polyphenolic polymers in their diet.

Another example would be for a consumer whose profile reveals a deficient value for gene SNP (variant) MTHFR C677T, which relates to homocysteine levels. This consumer would benefit from increasing their intake of folic acid.

The correlations between particular genetic variations and optimum nutritional support are based on **peer reviewed scientific literature**. Suracell maintains thousands of pages of study and reference data for review and analysis. Suracell is prepared to supply supporting studies and literature for the genetic science that supports the Suracell program, on further request from the committee.

Financial Issues Related To Suracell's Program

Because providing genetic testing is **not the purpose** of Suracell's business, Suracell **does not** make a financial profit from any DNA testing performed to provide information for analysis as part of its nutritional program.

Laboratories Performing DNA Testing for Suracell's Nutritional Program

The DNA test used by the laboratory to provide information for Suracell's nutritional program is performed by **SeraCare BioServices**, based in **Maryland.** SeraCare uses a **"home brew"** method for processing DNA samples submitted as part of Suracell's nutritional program.

Suracell has previously received confirmation from SeraCare that **CLIA** certification is in place for their facilities in Maryland.

Suracell Program Results

Suracell provides **clients and their health care professionals** with the results of the analysis provided by our program, and recommends nutritional supplements based on those results. To date, the percentage of Suracell clients receiving their results from a **physician or health care practitioner is 72%** -- which means that **28%** of Suracell clients have begun the program at home, and received their results in the manner of a direct to consumer approach. Clients who participate in this way are requested to select a Suracell affiliated physician or health care practitioner in their locality. If there are none available in their area, clients can choose to be assigned to the oversight of Dr. Giampapa, and may request that Dr. Giampapa provide any follow-up consultation needed to explain the analysis they receive, and to answer any questions that may arise as a result of their participation in the program.

Suracell's Clients

The Suracell program is designed for informed clients between the ages of **40 to 60,** because the processes affecting glycation, inflammation, methylation, oxidative stress and DNA repair are typically less efficient at this age, due to genetic inheritance, environmental exposures and lifestyle, but research indicates that improvements can still be made within this age range to enhance overall wellness. For example, simple dietary changes can significantly reduce oxidative stress levels which in turn can lead to improved overall wellness. The vast majority (approximately **85%**) of Suracell's customers are in the **40 to 55** age range.

Consumer Access to the Suracell Program

The Suracell program is recommended for consumers with the oversight of a licensed physician, genetic counselor or health care practitioner. Suracell's website lists the following organizations as additional resources for consumers:

National Society of Genetic Counselors

http://www.nsgc.org

National Human Genome Research Institute, NIH:

http://www.genome.gov

National Institute on Aging, NIH:

http://www.nia.nih.gov

The American College of Medical Genetics:

http://www.acmg.net

The American Medical Association:

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http://www.ama-assn.org

GeneClinics:

http://www.geneclinics.org

The American Aging Association:

http://www.americanaging.org

American Association on Aging:

http://www.asaging.org

Suracell Disallows Online Purchase of DNA Test Kits In Accordance With State Laws

Suracell's website is designed to **disallow online purchase** of DNA test kits in states which may not allow such tests to be purchased directly by consumers. There are approximately twelve states that may restrict testing in this way. Suracell **closely monitors** all existing laws that apply at the **state and federal level** related to Suracell's business, and can immediately make adjustments to comply with any new regulations.

Suracell's Consent Process

Suracell does not sell to anyone under the age of 18 and requires each customer to provide informed consent. The consent forms for the Suracell program are available online both to affiliated physicians and consumers. Suracell has established a comprehensive **FAQ** section on our website (link at http://www.suracell.com/faqs/) to ensure that consumer questions are answered and that the answers are clearly understood.

The consent process requires that customers actively consent to the testing of the samples they provide, in advance of any testing procedures, and, separately, that they consent to having their physician / health care practitioner receive the results of the analysis of such tests. While it is possible to provide the required consent online, most affiliated physicians print consent forms to discuss with their patients and keep completed printed versions in the patient files.

Notably, the laboratories performing the tests for Suracell destroy specimens upon testing completion, so the samples cannot be used for any other purpose.

Suracell's Privacy Protections

Suracell has a detailed, published privacy policy, available on our website at http://www.suracell.com/privacy.asp **. Suracell adheres to the FTC standards for privacy and protection of consumer information.** In addition, Suracell maintains compliance with the privacy and information provisions of the Health Insurance Portability and Accountability Act of 1996 (HIPAA) as well as the Gramm-Leach-Bliley Act (GLBA) and other applicable state and federal privacy laws. Suracell's internet system is housed in a HIPAA compliant data center, and uses technology methods such as SSL and PKE to secure and encrypt client data. Suracell's privacy policies and procedures are reviewed annually by TRUSTe, an outside privacy auditing agency.

Direct to Consumer Genetic Testing: Current State of the Business

By using an internet search engine, it appears that there are at least **fifty** or so companies

currently offering **direct to consumer** genetic (DNA) testing, particularly via the internet. There are roughly **five** categories of genetic tests being offered (in order of greatest number): paternity; genealogy; pre-natal; disease screening; nutrigenomics.

Suracell does not appear in the search results for "DNA testing" because this is not our business, and we do not promote Suracell in that way.

There are **several things** that become apparent as we search through the lists of companies offering these services: there is **no definitive way** for the consumer to determine the true **accuracy** of these test; there does not appear to be any "seal of approval" or oversight offered by any organization that would provide an **independent verification** of the usefulness and accuracy of the testing (although some companies appear to have accreditation by the American Association of Blood Banks); there does **not appear** to be a single, comprehensive standard for **follow-up, advice or support** offered to consumers with regard of the outcome of these tests.

Suracell's Concerns Related To Direct To Consumer Genetic Testing

The overriding concern about direct to consumer testing must be the protection of the public from misleading and inaccurate information. The most important aspect of this is the **accuracy** of the testing and results provided. Consumers may be making life-altering decisions based on the results of these tests, particularly in the area of paternity, disease screening and pre-natal screening. Therefore, the public needs to be **protected** by oversight and validation of the laboratories providing test results. **An expansion of**

the CLIA standard to include the sub-specialty of genetic testing would be a useful step in this process.

Suracell's Views On Article: Federal Neglect: Regulation of Genetic Testing:

Gail H. Javitt, Kathy Hudson (**"Issues in Science and Technology"**, Spring 2006).

This article, specifically referenced by the Senate Committee on Aging, on which we were asked to provide comment, appears to raise several salient points related to direct to consumer DNA testing:

Suracell is in agreement with the following points raised by the article:

- the FDA should expand its oversight of ASRs
- there should be a specific CLIA standard for the sub-specialty of genetic testing
- there needs to be governmental oversight of the accuracy and predictive value of tests, particularly with regard to pharmagenomic tests that involve disease prediction
- the FTC should closely examine advertising claims made by companies offering direct to consumer DNA testing, to make sure the advertising is not misleading, or making false or exaggerated claims about the accuracy and meaning of test results

Suracell's Recommendations

Suracell knows of **no way** in which the providing of genetic and nutritional information

to clients as part of Suracell's nutritional program can result in any harm to those clients, as long as the accuracy and confidentiality of that information is maintained.

Suracell **strongly believes** that informed consumers can benefit from knowing their genetic variance as it relates to the aforementioned metabolic processes because such knowledge enables them to make **dietary and behavioral changes** to improve their overall wellness.

In addition, Suracell believes that in order for the benefits of new genetic knowledge and technologies to be realized, the public **must be assured** that genetic testing is accurate. Suracell believes that **increased governmental oversight is necessary** to **protect the public** from companies selling inaccurate tests or services.

Suracell recognizes and **recommends** that establishing a genetic testing specialty certification within CLIA may be an **effective strategy** to achieving oversight of genetic testing, and is supportive of this action. Furthermore, Suracell welcomes and supports actions at the federal level to provide consumer protection and assurance in the area of genetic testing, believing that such actions would be beneficial to companies, such as Suracell, that seek to provide accurate and ethical services to the public.

It is Suracell's belief that the federal government should **lead the way**, even if congressional action and **further legislation** is needed. Suracell **voluntarily** offers its services in support of any such effort, and is committed to making whatever adjustments

or changes might be necessary to comply with any new regulations or provisions of law.

Concluding Statement

Suracell thanks the committee for the opportunity to submit testimony to the Senate Committee on Aging, and is happy to answer any further questions it may have of Suracell, and supply any further assistance that may be requested.

Suracell's team looks forward to reviewing the report of the GAO on the issue of direct to consumer genetic testing, and the recommendations made therein. If requested so by the Committee, we would be happy to provide written comments in response to the Report's findings and recommendations, once we have had the opportunity to review the documents.

I would be happy to respond to any questions the Committee Members might want me to address.

Kristopher King - Biography

Kristopher King has been prominent in the business world for many years, during which time he has been a consultant to some of the world's largest companies, as well as founding several high-growth companies himself.

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Kristopher has utilized his experience and skills to create successful technology focused companies in both the technology service and product areas. He has served as CEO of several of these companies.

Kristopher currently sits on several boards, including the Boy Scouts of America, and Norwalk Community College Foundation Board.

He attended Fairfield University in Fairfield, Connecticut.

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SURACELL'S RESPONSE TO ISSUES RAISED AT THE UNITED STATES SENATE SPECIAL COMMITTEE ON AGING HEARING - 7/27/2006

"Direct To Consumer Genetic (DNA) Testing"

July 31, 2006

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On July 27, Suracell voluntarily participated in a Senate Special Committee on Aging hearing on the subject of genetic testing. Suracell had anticipated that the hearing would involve discussion of the scientific issues involved in genetic testing, and a discussion of the ethical and legal safeguards appropriate to protect consumers from misuse of their genetic information. Instead, Suracell, as well as other members of the industry panel appearing in front of the committee, were presented with the contents of a GAO report that they did not have access to prior to the hearing, which contained allegations that the information provided to clients by Suracell and others is ambiguous, and based on unproven science.

The GAO report references nutrigenetic tests purchased by GAO investigators through the internet, and then refers to the companies supplying the tests as "Websites 1, 2, 3, and 4." Suracell was designated as "website 4." However, the bulk of the report and the testimony focused on "Websites 1, 2, and 3." Suracell provides nutraceutical products for its customers, and recommends tailored nutraceutical programs to customers based upon nutrigenetic testing, and a lifestyle questionnaire that provides environmental information. As a nutraceutical company, we are disappointed that Suracell was included in the same category as "Websites 1, 2, and 3", who are simply marketers of genetic tests.

The five companies that provided testimony as part of the industry panel before the Senate Special Committee on Aging were not provided with an opportunity to review the GAO report prior to testifying on July 27, 2006. When Suracell requested a copy of the GAO report, we were advised that it would not be released prior to July 27, 2006. Despite various efforts, we were not able to obtain a copy of the report until Kris King (CEO of Suracell) walked into the committee hearing room the morning of the hearing. It became obvious

during the testimony by the government witnesses that they had reviewed the report prior to their testimony. It seems that certain members of the press may also have had access to the report prior to the hearing. However, now that we do have a copy of the GAO report, we intend to follow up with the GAO and seek the opportunity to discuss those aspects of the report that pertain to Suracell and to correct any inaccurate information.

In addition to the GAO's testimony, Kathy Hudson, Director of the Genetics and Public Policy Center at Johns Hopkins University testified at the hearing, expressing views that Suracell wholeheartedly agrees with. She stated, as follows: "Genetic testing is becoming an increasingly important part of medical care. Once the province of esoteric testing laboratories and limited to rare diseases or conditions, genetic tests now are being offered by a growing number of clinical laboratories for an increasing number and variety of conditions or health risks. The number of tests has increased 10-fold over the last decade and continues to grow. Today, there are genetic tests clinically available for nearly 1000 diseases, with hundreds more in development. Genetic tests can be performed at any stage of the lifecycle: on fetuses during pregnancy, newborn babies, children, and adults of all ages.

Genetic tests provide information -- information that can be used to diagnose disease, to predict risk of future disease, and to guide decisions about whether to undergo a medical procedure or take a particular drug or dosage of a drug. Increasingly, genetic testing will be used routinely in medical care to alert us to future health risks and guide early prevention and intervention. Genetic testing also will be used to help doctors prescribe the right medicine at the right dose for individual patients, thus avoiding costly and sometime tragic adverse drug reactions."

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Suracell provides clients with information enabling them to optimize their general wellness, via dietary supplements, diet and lifestyle changes. One of the three components of Suracell's personalized nutritional program is an analysis based on information from the results of a gene variant test that identities twenty-six gene variants associated with the efficiency of glycation, inflammation, methylation, oxidative stress and DNA repair. Most of Suracell's clients are referred through physicians.

The genetic test used by Suracell to guide its clients in their choice of supplements has been validated by industry standards, and the interpretation of the test is based on peer-reviewed scientific literature. Suracell is guided by a scientific advisory board comprised of specialists in genetics, microbiology, gerontology as well as several clinical MDs. It is unfortunate that the GAO did not ask to see or review the scientific literature on which Suracell's test interpretation is based, before reaching conclusions. While Suracell does not accept that the information provided to consumers is ambiguous, Suracell's test interpretation reflects the same uncertainties that exist in the scientific literature.

Another topic of discussion by the Senate Committee was the handling of a person's genetic information. Suracell was disappointed that the hearing did not acknowledge the importance of the safeguards that Suracell has put in place to help ensure that its clients' personal information is protected, and that its clients' DNA samples are destroyed after testing. Suracell has a robust privacy policy and does not permit testing without informed consent. Further, Suracell is committed to ongoing education of its clients.

The hearing also focused on the need for increased federal regulation of genetic testing, a perspective that Suracell shares. Suracell offered several recommendations for strengthened federal oversight at the hearing.

There is no debate that genetic testing holds great promise to improve health care and consumer well-being. Suracell believes that consumers have a right to obtain information on their genetic make-up. In circumstances where genetic testing is intended to diagnose serious diseases, the involvement of a health care professional is absolutely necessary. In circumstances in which the test provides information to help consumers maintain and improve their well being through life style changes, consumer directed testing is appropriate.

As a nutraceutical company, Suracell's focus is on providing clients with quality products. Suracell products are manufactured under a comprehensive quality system based on Federal Current Good Manufacturing Practices (cGMP). Suracell's manufacturing facility has been audited and quality approved by key industry certifying bodies, including:

- GMP Certificate - Academy of Clinical, Environmental, Research and Information Services (ACERIS)
- GMP "A Rating" - National Nutritional Foods Association (NNFA)
- Certification by Australia's Therapeutic Goods Administration (TGA)
- Kosher certification (all major authorities)

During the hearing, the Chairman of the committee, Senator Smith, commented that similar supplements could be purchased at Rite Aid for significantly less than is being charged by Suracell. While it is true that Suracell's nutraceuticals are more expensive than Rite Aid's, for about the cost of a daily venti latte, Suracell consumers can take advantage of

high quality, American made nutraceuticals. Our clients have a clear choice for their supplements: the cheaper option of buying from a drugstore or supermarket, where stringent manufacturing practices and quality control are not required, or even consistently used by many product manufacturers, or the more expensive option of buying Suracell products, which do meet these criteria. Suracell's loyal clientele have chosen to spend more, based on what they perceive as Suracell's advantages: high quality, scientifically formulated products, backed by scientific research.

Senator Smith also made a comment during the hearing suggesting that Dr. Giampapa is less than qualified to lead a nutraceutical company because he is a "plastic surgeon". In fact Dr. Giampapa is well qualified in the field of wellness and age management based on dietary supplements. Dr. Giampapa was one of the six founding members of the American Academy of Anti-Aging Medicine - A4M, which now has over 5,000 members who are MDs. He served as *President* of the American Board of Anti-Aging Medicine - ABAAM, the A4M branch that writes and administers the certification exam for doctors wishing to specialize in Anti-Aging Medicine. He has written five books including a medical text book on Age Management and has published research on the use of nutraceuticals and their effects on cellular aging and DNA. He is also a Board Certified Plastic Reconstructive Surgeon and Assistant Clinical Professor of Plastic Surgery at the University of Medicine and Dentistry of New Jersey. He is the *President* and *Medical Director* of the Plastic Surgery Center Internationale and Giampapa Institute for Anti-Aging Medical Therapy.

We agree with Senator Smith that genetic testing holds great promise and agree that accuracy and validity of genetic tests are important. It is not our intent to mislead consumers

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but rather to allow and enable consumers to be better educated, more proactive and make better choices in their lifestyle to improve the quality and duration of their health.

It is the intent of Suracell to continue to cooperate with the Committee, the GAO and others and provide additional science and background information that will result in a better understanding of the company and its products.

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Mr. Ramarathnam.

STATEMENT OF NARASIMHAN RAMARATHNAM, PRESIDENT, GENOX CORPORATION, BALTIMORE, MD

Mr. RAMARATHNAM. Thank you, Mr. Chairman. My name is Narasimhan Ramarathnam. I know it is pretty complicated and for the sake of convenience, people know me as Rama.

The CHAIRMAN. Dr. Rama?

Mr. RAMARATHNAM. Dr. Rama. That is right.

The CHAIRMAN. OK.

Mr. RAMARATHNAM. I am the president of Genox Corporation, a position that I have held since November 1998. I understand that you have been provided with a copy of my written testimony and attachments that are to be made part of the record.

I would like to take this opportunity to describe briefly the history and mission of Genox. Genox is a small biotechnology company located in Baltimore, MD. The company was organized in October 1991 by a small group of U.S. investors, along with Dr. Richard Cutler and his son, Roy Cutler. Dr. Cutler is a well-known scientist in the field of aging. Prior to founding Genox, Dr. Cutler spent 18 years as a research chemist at the National Institute on Aging, which is a division of NIH.

The late Dr. Hirotomo Ochi, the founder of Nikken Foods and Nikken groups of companies in Japan, was asked to invest in Genox shortly after the laboratory was established. Prior to investing in Genox, Dr. Ochi had already established the Japan Institute for the Control of Aging. We call it JaICA. Dr. Cutler served as the president of Genox from January 1995 until he resigned in November 1998.

During the past decade, Genox has served the scientific community by providing to researchers products and services for the measurement of biomarkers that would indicate oxidative stress levels. In layman's terms, oxidative stress is like a see-saw. We have damage on one side and the anti-oxidative defense forces on the other side. The moment a tilt takes place toward the damaged side, the aging process sets in, leading to the gradual loss of physiological functions normally later in life.

Genox sells this patented kit which is made by JaICA. This kit is normally sold to scientists and researchers for them to use in their laboratories. Using this kit, the researchers can measure the DNA damage biomarker 8-OHdG, 8-hydroxy deoxyguanosine. Please note that this test kit is not the so-called home test DNA kit. It should not be used by anyone at their homes. It does not measure DNA directly. One has to have special skills, and also will need special equipment to use this kit. Once again, this is not a home test kit.

Among the many institutions using this kit are OXIS Health Products, located until last year in Portland, OR; the Medical College of Wisconsin; NYU; the University of North Carolina; University of Pennsylvania; Yale; Harvard; Johns Hopkins University; VA Hospital; and U.S. EPA. We have submitted to this Special Committee a list of 28 publications by scientists who have used this product that will demonstrate the importance and utility of this kit.

Genox also offers analytic services to scientists who are involved in basic and applied research. These research scientists lack either the necessary equipment or expertise needed to measure 8-OHdG in their research samples. Through the provision of its analytic service, Genox enables more extensive research on aging than would otherwise be possible.

The major institutions whose researchers use Genox analytic services are the University of Pittsburgh, Johns Hopkins University, Colorado State University, Harvard School of Public Health, VA Hospital, and the National Institute on Aging. I have attached to my testimony copies of seven publications by scientists who have used Genox services.

Take, for example, the interesting studies of oxidative stress in individuals trained at moderate and high altitudes. The work was done by Professor Eldon Askew, of the University of Utah. This research is of great significance for our armed forces. Every time scientists like Dr. Askew call us and request our service, it makes Genox and me personally grow younger and not older.

In closing, again I want to thank the Committee for inviting me to testify and commend you, Mr. Chairman, for holding this hearing. I will be happy to answer any questions you may have for me.

Thank you.

[The prepared statement of Mr. Ramarathnam follows:]

Testimony of Narasimhan Ramarathnam,
President, Genox Corporation
Before
Senate Special Committee on Aging
Thursday, July 27, 2006

Mr. Chairman and Committee Members:

My name is Narasimhan Ramarathnam. For convenience, I am generally known by my professional colleagues in Canada and the United States as Dr. Rama. I am the President of Genox Corporation, a position that I have held since November 1998. Genox is a small biotechnology company located in Baltimore, MD. The company was organized in October 1991 as a Minnesota Corporation by a small group of investors, along with Dr. Richard G. Cutler and his son, Roy Cutler.

Dr. Cutler is a well-known scientist in the field of molecular gerontology. Prior to founding Genox, Dr. Cutler spent 18 years as a research chemist at the National Institute on Aging (NIA) of the National Institutes of Health (NIH). He is internationally recognized for both his theoretical and his experimental work on the biology of aging and longevity. A list of his published research papers is attached. The Genox research laboratory was set up in Baltimore to be near the residences of Dr. Cutler and his son.

The late Dr. Hirotomo Ochi, the founder of Nikken Foods and the Nikken Group of Companies, was asked to invest in Genox shortly after the laboratory was established. Nikken Foods is a major supplier of natural flavorings and seasonings to food processing industries all over the world. Dr. Ochi had a life-long interest in the scientific study of aging processes. Prior to investing in Genox, Dr. Ochi had established a laboratory to pursue scientific work through the Japan Institute for the Control of Aging (JaICA), a division of Nikken Foods. His scientific temperament and interest in Dr. Cutler's scientific work on molecular gerontology while Dr. Cutler worked at NIH, led Dr. Ochi to invest in the establishment of Genox at Baltimore and continue to fund its operations. Dr. Ochi passed away in November 2005, but left a legacy in Japan and the United States for the continuing pursuit of scientific research on the processes of aging.

Dr. Cutler served as President and CEO of Genox Corporation from January 1995 until he resigned in November 1998 to pursue aging research at Kronos Science Laboratory in Phoenix, Arizona. His son, Mr. Roy Cutler, following his father's footsteps, now works for NIA at NIH.

During the past decade Genox has served the scientific community by providing to researchers products and services for the measurement of biomarkers that indicate oxidative stress levels. Oxidative Stress (OS) is a general term used to describe the steady state level of oxidative damage in a cell, tissue, or organ, caused by the reactive oxygen species (ROS). This damage can affect a specific molecule or the entire organism. Reactive oxygen species, such as free radicals and peroxides, represent a class

of molecules that are derived from the metabolism of oxygen and exist inherently in all anaerobic organisms. ROS can be generated internally or externally. Most ROS are by-products of normal metabolic reactions, such as energy generation from mitochondria. External ROS includes exposure to cigarette smoke, environmental pollutants and consumption of alcohol, to name three examples.

In layman's terms, oxidative stress is like a see-saw, a well-maintained balance between the oxidative damage that constantly occurs inside our body as a result of normal oxygen metabolism and the counterbalancing forces of the inherent anti-oxidative defenses in our body. When a tilt towards the damage side of the see-saw occurs, the aging process sets in, leading to the gradual loss of physiological functions, normally later in life.

Genox research tools include an Enzyme Linked Immuno-Sorbent Assay (ELISA) Kit, to be used by scientists in their laboratories, for their own research purposes. This kit was developed at JaICA, our parent company in Japan. JaICA holds the Japanese Patent (No. 3091974) for this kit. The kit helps scientists measure the DNA damage biomarker, 8-hydroxy-2'-deoxyguanosine (8-OHdG). The kit is not for "home test" applications. It does not analyze DNA directly. Very specialized skills are required to measure the precise volume of samples and the appropriate reagents needed for the analysis. Specialized equipment is also required, including a multi channel pipette, an incubator to maintain constant temperature during the analysis, a special microplate reader and analytical software to measure the samples after the experiment is completed.

The ELISA test kit is widely used by scientists all over the world. Among the many research institutions using the ELISA kit and are OXIS Health Products, located until last year in Portland, Oregon; the Medical College of Wisconsin; New York University; State University of New York; University of North Carolina at Chapel Hill; University of Pennsylvania; Penn State University; Yale University; Harvard University; Johns Hopkins University, and Emory University. Scientists working in federal research institutions such as Veterans Administration Medical Center, and United States Environmental Protection Agency have also purchased and used the kit for their work. Attached is a list of 28 publications by scientists who have used this product that demonstrate the importance and utility of this kit and Genox's services for the advancement of scientific research on the processes of aging.

Genox also offers analytic assay services to scientists who are involved in basic and applied research. The data provided by Genox enables these scientists to understand the mechanism of aging and investigate the causes for oxidative stress-mediated diseases. These research scientists lack either the necessary equipment or expertise to measure the levels of 8-OHdG in their research samples. Through the provision of its analytic services Genox enables more extensive research efforts on aging than would otherwise be possible.

The major institutions whose researchers use Genox's analytic services are the University of Pittsburgh, Johns Hopkins University, Colorado State University, Harvard School of

Public Health, Penn State University, Veterans Administration Hospital and the Gerontology Research Center or the National Institute on Aging of NIH .

In April of this year, I attended a conference on Experimental Biology held at San Francisco. I learned from scientists there that they want additional products from Genox. Many researchers are now asking for a method for analyzing protein oxidation. Work is already underway at JaICA to develop a new monoclonal antibody against 3,5-DiBrY, a protein oxidation biomarker.

I have attached to my written testimony seven publications by scientists who have used Genox services. These studies represent the type of work that our services facilitate. Take for example, the acknowledgement made by Professor Eldon Askew, Director of Division of Foods and Nutrition, of the University of Utah. He studied control of oxidative stress in individuals trained at high altitudes, research of great significance to the armed forces. Dr. Lloyd Greek of the University of Colorado Health Sciences Center, in his testimonial, has also emphasized the significance of the measurement of 8-OHdG produced in individuals who were subjected to diagnostic radiology (medical imaging) studies. Every time scientists like Dr. Askew and Dr. Greek call us and request our services, it only makes Genox and me personally grow younger and not older. The primary mission of Genox is to serve the scientific community so that the mechanism of aging and age-related disease processes will become easier to understand and interpret.

In closing, I again want to thank the committee for inviting me to testify, and commend you, Mr. Chairman, for holding this hearing. Our late founder, Dr. Ochi used to believe in three basic principles, "I am OK You are OK," "Affirmative Philosophy," and "Good Science Makes Good Business." Let's all take a broader perspective in life, and work together towards the betterment of mankind.

I will be happy to answer any questions you may have for me.

The CHAIRMAN. Mr. Rama, your kit may be entirely valid when used by medical institutions and physicians, but what I am concerned about is your lab. It is not CLIA-certified. Is that correct?

Mr. RAMARATHNAM. That is correct, sir. Our mission is to be of service to the scientific community who are involved in basic and applied research related to oxidative stress and aging.

The CHAIRMAN. Why would your lab not be able to pick up synthetic urine?

Mr. RAMARATHNAM. We treat all samples as samples. We do not classify whether it is natural urine, whether it is synthetic urine. When we are able to report or detect the levels of 8-OHdG, we will give the value. If it is not detectable—we will report it as not detectable. We cannot identify that it is artificial or natural urine.

The CHAIRMAN. Are you aware your customers, some of whom are selling their kits and using your lab, are making representations that you have these abilities?

Mr. RAMARATHNAM. Our research report clearly says it should be used as a research tool in the study of oxidative stress related to aging and disease—oxidative stress related disease and aging. Genox Corporation assumes no responsibility for the use of this report for diagnosis, treatment, cure, or prevention of any health-related condition.

The CHAIRMAN. Well, you disclaim using genetic tests, but your company's website clearly markets in-house tests for assessing DNA damage.

Mr. RAMARATHNAM. That is correct, sir. We measure the end product of oxidative DNA damage. We do not measure DNA by itself.

The CHAIRMAN. So you are saying that assessing DNA damage is something different than performing—is no part of a genetic test?

Mr. RAMARATHNAM. It is not related to genetic testing.

The CHAIRMAN. Now, I understand your lab is not just dealing with research because it is running tests on samples received straight from consumers from Suracell. Is that correct?

Mr. RAMARATHNAM. Our understanding was we were—I mean, Suracell would use this report only for their product development. It should not be used for treatment of any disease or curing any illness. So all these subjects or volunteers who would send their samples to us—we will test them and report back to Suracell as a research tool to help them in their product development.

The CHAIRMAN. You are receiving their samples directly from Suracell's customers? They come right to you?

Mr. RAMARATHNAM. Yes, sir.

The CHAIRMAN. Are you aware how they are representing your results from those tests?

Mr. RAMARATHNAM. No, we are not aware of that.

The CHAIRMAN. Do you have any concern with that?

Mr. RAMARATHNAM. Yes, we do.

The CHAIRMAN. I think you should. That is why you are here today.

Mr. RAMARATHNAM. Thank you, sir.

The CHAIRMAN. We thank you for being here today.

Howard Coleman.

STATEMENT OF HOWARD COLEMAN, FOUNDER AND CHIEF EXECUTIVE OFFICER, GENELEX CORPORATION, SEATTLE, WA

Mr. COLEMAN. Thank you, Senator. Thank you very much for inviting me here today. I share your concerns about the quality of the results that are produced by this industry as it very rapidly grows. I very much support the regulatory process.

Genelex is a DNA testing company that I founded with our laboratory director in 1987. We have been providing direct-to-consumer DNA testing for more than a decade, beginning with paternity testing in the mid–1990's. In 2000, we began to do pharmacogenetic DNA drug reaction testing, and then in 2002 the nutritional genetic testing.

We are a CLIA lab, and we are also accredited by the American Association of Blood Banks Parentage Testing Committee. For 5 years, we were accredited by the American Society of Crime Laboratory Directors' Laboratory Accreditation Board. I bring those accreditations up because they represent the best in quality assurance programs in the DNA field at this time.

One of the reasons that those programs were so successful and continue to be successful is because they were peer-initiated and done in a cooperative fashion. Federal, State and local government worked together with industry. The College of American Pathologists was involved, the National Institute of Standards and Technology was involved, and as a result we came out with excellent programs that are ongoing today.

I am disappointed in the GAO report based on what I heard today. I regret that we did not have the opportunity to see this report beforehand. There are a lot of points in this that could be clarified had the GAO come to us and said, "here is what we found out and here are the conclusions that we are making" and given us the opportunity to comment.

One of the things that I am familiar with is the dietitian they are speaking of, I am guessing, is a dietitian that we work with. She is adamantly opposed to selling supplements, and we don't sell supplements either because it is an intrinsic conflict of interest for us as the DNA tester. She certainly would not contact someone if they weren't seeking, or based on telephone calls to us and questions to us, had not expressed a need for further information. This perhaps addresses the statement that the reporting is ambiguous. We provide this extra level of support in order to help people interpret the test results and put them into action.

In general, these tests—and I want to include the pharmacogenetic testing we do are the wave of the future in terms of gaining benefit from the Human Genome Project. These tests are in various ways on the cutting edge of science, and while some of them may not be proved to the standards required to prescribe a dangerous drug to someone, for altering your lifestyle in terms of your diet and other factors, they can be very useful.

I make that statement based on the fact that we have done this testing for hundreds of people and the feedback we get from people is that these tests help them make the behavioral and lifestyle changes they need to do to control risk factors that over a period of decades lead to major diseases.

The CHAIRMAN. Do those people take those tests from your lab at the direction of a physician?

Mr. COLEMAN. The nutritional genetic testing, generally not.

The CHAIRMAN. Do you think they should?

Mr. COLEMAN. Yes, very much so, if——

The CHAIRMAN. But they don't necessarily?

Mr. COLEMAN. No, sir, they do not.

The CHAIRMAN. They are being, frankly, sold these tests without the context of how to really take advantage of what you call the fruits of genetics?

Mr. COLEMAN. I don't think that is true, sir. That is why we work with a certified nutritional specialist. That is why the reports provide a level of detail around these individual factors.

The CHAIRMAN. So you just simply have a difference of opinion with the earlier witnesses from Johns Hopkins that, to be meaningful, genetic testing needs to be done in a more comprehensive fashion?

Mr. COLEMAN. I wouldn't describe that as the nature of the disagreement I have. The disagreement I have is with the conclusions that the GAO reached, and from listening to that testimony I regret that we did not have an opportunity to see this report so that we could address the specific items in this report.

The CHAIRMAN. Well, that is fair enough. I mean, you can have a difference of opinion. That is allowed in America.

Mr. COLEMAN. Sure.

The CHAIRMAN. As a CLIA-certified lab, do you have concern with what you have heard this morning about how loosely this enterprise is being engaged with?

Mr. COLEMAN. Yes, sir, I do. I support your efforts here and I think we need to have more regulation. I think that, in general, now most of the testing is done in CLIA labs and in a quality fashion. The people that I know in the industry are very conscious and aware of this, but I think that we are going to see an explosion of people coming into this field in the fairly near future and I think it is very important that there are some regulations in place to see that that is done in an orderly fashion so that people can gain the benefits of this testing, as they do now, in the most efficient and beneficial fashion.

The CHAIRMAN. Howard, you have one position and you are entitled to a difference of opinion. My struggle here is just simply that your genetic tests—if they are accurate, how do you explain the results from 14 profiles based on only two DNA samples?

Mr. COLEMAN. Senator Smith, I would like to see those reports and be able to go over that and understand it.

The CHAIRMAN. Well, I hope you will. I mean, this Committee is following congressional protocol. GAO is following their protocol. You ought to get into this because, frankly, if you are coming up with results from 14 profiles based on two DNA samples that are all varied, I think you ought to have some very real concern about that.

Mr. COLEMAN. I want to know why, exactly. I want to know why that is.

The CHAIRMAN. So you can understand why the GAO would come to their conclusion?

Mr. COLEMAN. Yes, I can, and I think that they should have come to us to say, here are our conclusions, what is going on here, because there may be explanations for this.

The CHAIRMAN. Well, I encourage you to stay in contact with this Committee. We would like an answer, too. I mean, to me, it is per se a problem if you have got only two DNA samples and 14 profiles that are different.

Mr. COLEMAN. It could be based on differences in the lifestyle questionnaire. Until I would have an opportunity to review those reports—and I would like to involve Dr. Gill-Garrison in that process—it is impossible to say.

The CHAIRMAN. Well, I think we have demonstrated why we need to get into this as a Government to provide some standards so that the public is protected and you can pursue a credible enterprise, but we don't have that right now.

Mr. COLEMAN. I very much welcome those efforts. If I could continue?

The CHAIRMAN. Please.

Mr. COLEMAN. In the more medicalized arena of the drug reaction testing, the pharmacogenetic testing that we have been doing direct to the public since 2000, this is the single greatest opportunity to improve the health care of the aging because of the huge, as the FDA describes it, adverse drug reaction problem. They describe it as a major solvable public health problem, and that is because half of the people that we test have a variation in their genetics that alter how they are able to process about half of the most commonly prescribed meds.

We are talking about several classes of heart medicines, anti-depressants, anti-psychotics, pain meds, anti-diabetics, and the list goes on. Those DNA test, particularly when combined with drug interaction software that can help interpret those results, is a very powerful solution to the adverse drug reaction problem. There is an embarrassing gap between our knowledge in that area and its application in medicine, and that is one of the reasons that we sell those tests direct to the public.

We warn people, we tell people on everything, don't change your meds without going to your doctor. But many of our people come to us who have had a history, a very long history of problems with meds, and these problems have not been addressed by their physicians or their other health care providers. We do the genetic test and this shows why they have had these problems all these years and leads them to work out a solution with their physician.

The CHAIRMAN. Should I be worried, Howard, about the privacy of your customers?

Mr. COLEMAN. Well, I would say that coming to a company like ours is a way for you to protect your privacy. If you go to your doctor and order one of these tests, then you don't have control of that information. That has gone into the health care records system, and HIPAA notwithstanding, I think people have concerns about the security of that information. If you come to a company such as ours, then that information will remain secure. It is your property and short of a court order, we under no circumstances would release that information to anyone.

The CHAIRMAN. But I understand in reviewing your company that your questionnaire doesn't even ask if they have medications or existing diseases to warn consumers about risk. Am I wrong on that?

Mr. COLEMAN. The questionnaire for the nutritional genetic test you are asking about?

The CHAIRMAN. Yes. You don't even ask if they are on medications for existing diseases.

Mr. COLEMAN. I look forward to the day when we have a more comprehensive program and we combine the medical aspects with the more nutritional aspects. But I think that in designing this test, Sciona has wanted to draw a very sharp line between what is medical and what is not, and I think they have been very careful not to stray into the medical arena with their test.

The CHAIRMAN. Well, I think you have just made the point that Dr. Hudson was making from Johns Hopkins. You have got to have actual and you have got to have legitimate clinical studies.

Mr. COLEMAN. Well, you have to have clinical studies. You can prove this stuff to death, though, and it will never get out to the public. The use of it will never be made. The fact is people find this information useful now and it does help people.

The CHAIRMAN. But it can't be very useful if you don't even ask them if they are on medication, if you don't know anything about their environment, their medical history.

Mr. COLEMAN. When we do the pharmacogenetic testing, we have a questionnaire that we send to people asking all the meds that they are on. We have a software that they can access in a password-protected fashion. They can put all their meds in that program and get a report that they can take to their doctor.

The CHAIRMAN. But you are going to beef up your questionnaire, though.

Mr. COLEMAN. Pardon?

The CHAIRMAN. You are going to beef up that questionnaire to get a more comprehensive background on somebody?

Mr. COLEMAN. The nutritional genetic——

The CHAIRMAN. Yes.

Mr. COLEMAN. I don't have control over that questionnaire, sir.

The CHAIRMAN. Who has control of that?

Mr. COLEMAN. Sciona does.

[The prepared statement of Mr. Coleman follows:]

United States Senate Special Committee on Aging
July 27, 2006
Written testimony of
Howard Coleman
Founder & CEO
Genelex Corporation
Seattle, Washington

Leading scientists and clinicians predict that the widespread adoption of DNA testing technologies will bring revolutionary improvements to long-term health, medication safety and efficacy. This will open an era of personalized medicine, thereby fulfilling the promise of the Human Genome Project. Accelerated adoption of existing, yet underused, pharmacogenetic DNA drug reaction testing, combined with evidence-based drug interaction software, is the most important existing opportunity to personalize and improve U.S. senior healthcare. The routine use of this technology by physicians leads to evidence-based prescribing practices that could save thousands of lives every year, lead to improved quality of life for many senior citizens, and save money. (See attached DNA and Adverse Drug Reactions Fact Sheet.) The ability of consumers to purchase DNA Drug Reaction Testing directly is an important force driving the adoption of this life-saving technology.

> "...the incorporation of pharmacogenetics into clinical medicine is likely to have a great effect on public health in the near future."
>
> Yoseph Caraco, MD NEJM 351; 27 2004

Direct to Consumer DNA Testing

Many DNA tests, including paternity, DNA drug reaction, nutritional genetic, and some medical genetic tests are currently available directly to the public. Purchasing these tests directly, bypassing their physicians, is the only way patients have to control the entry of this information into the healthcare records system. In many instances, direct ordering of the tests also saves consumers money. It is important for citizens to continue to have this right, given the sensitivity of genetic information and the lack of confidence people may have in the ability of the healthcare records system to protect their privacy.

Until the mid-1990s, most parentage testing was ordered by doctors or lawyers. When the testing became available direct-to-the-public there was concern voiced that this would be problematic. By now tens of thousands of people have obtained the benefits of DNA parentage testing, at lower cost and in the privacy of their homes, without the development of significant problems.

Need for Interpretive Services

All DNA testing requires appropriate reporting and interpretation services in order for consumers to take action based on test results. In DNA Drug Reaction Testing the lack of appropriate interpretive software has, until recently been a major barrier to the adoption of the testing by the medical community. The many combinations of interacting genotypes and changing medication regimens require complex, evidence-based software such as GeneMedRx. Recently introduced by Genelex, GeneMedRx is a genetics-enabled drug interaction software program created by physicians for physicians to help them apply DNA Drug Reaction Testing results. Trained personnel, whether pharmacogenetic experienced physicians, certified nutritionists, genetic counselors, or trained client service personnel need to be available to consumers. Currently, laboratories providing DNA testing appear to be doing a reasonable job of providing these services and are not providing results in a fashion that could be harmful to patients. As the field

grows it will be important to ensure that the level of information provided to clients and their providers continues to improve and remains at a high level.

DNA Testing Regulation

Since the commercialization of DNA testing began two decades ago, the development of quality standards and comprehensive quality assurance programs has been widespread throughout the disparate public and private sector enterprises producing and using DNA test results. In 1992, for example, the American Association of Blood Banks Parentage Testing Committee initiated the first comprehensive quality program available for DNA testing by inspecting and accrediting DNA parentage testing laboratories.

Medically used DNA testing is covered by CLIA (clinical laboratory improvement act) regulations. The development of CLIA regulations that address DNA Testing as a specialty is a welcome natural evolution of the regulatory process. Most testing is done as "home brew" which means the test has been validated to CLIA standards by the testing laboratory. These tests are not subject to FDA regulation. The FDA is becoming involved by the approval of DNA testing instruments and reagent kits which are regulated as medical devices. DNA testing is designated as high complexity by CLIA. The growing availability of FDA approved DNA tests allows it to be performed in lower complexity settings. It is not appropriate for academic research laboratories to perform medical genetic testing for patients without being CLIA licensed.

Nutritional Genetic Testing

Recently Nutritional Genetic Testing has become available to the public over the internet, through multilevel marketing organizations and retail stores. These tests are designed to help people personalize their diet and supplement programs in order to reduce the incidence of dietary and life-style induced risk factors that over a period of decades can lead to major disease.

Although sometimes criticized by academics scientists as being premature, nutritional genetic testing is proving useful to clients by helping them make the long-term behavioral changes required to optimize health. As the testing results in the development of individualized programs it tends to improve compliance and permits clients to resist the many fads that permeate the nutrition and weight loss fields.

> "...for people who are already overweight, the public health interventions aimed at the general population are not a complete solution. ...public health needs to also seek new approaches—such as considering genetic factors in risk factor assessment and intervention design – to more thoroughly address this complex problem..."
> *CDC (US Centers for Disease Control and Prevention) 2005.*

Currently, most of this testing is done in CLIA licensed laboratories, even though it may not be subject to CLIA regulation. It is important that as the field grows and new players enter the market place, that current truth in advertising and other consumer protection legislation is adhered to.

Genelex Company Background

Since starting in 1987, Genelex has become a world leader in direct-to-consumer DNA testing by commercializing proven but generally unavailable tests. Throughout the 1990s Genelex was recognized as a pioneer in forensic and paternity DNA testing. In 2000 the company entered the field of personalized medicine with the first launch of direct-to-consumer pharmacogenetic testing for the prevention of adverse drug reactions. In 2002 Genelex was the first to launch nutritional genetic testing in the U.S. In 2005, with the launch of the genetics-enabled GeneMedRx drug interaction software, Genelex began providing the first comprehensive personalized prescribing program available.

Genelex has been accredited by the AABB Parentage Testing Committee in DNA parentage testing since 1992, the American Society of Crime Laboratory Directors Laboratory Accreditation Board from 1998 to 2003, is Washington State Medical Test Site No. MTS-3919 CLIA No. 50D0980559 and has contributed to the validation of National Institute of Standards and Technology (NIST) Standard Reference Materials.

The CHAIRMAN. OK, back to Sciona. Ms. Gill-Garrison, your company was shut down in the United Kingdom.

Ms. GILL-GARRISON. It was not shut down. We made a commercial decision to move the company to the United States in response to consumer demand. We found that people in the United States, in North America in general, were much more interested in taking a proactive role in their own health and well-being.

The CHAIRMAN. So you are still doing business with the British?

Ms. GILL-GARRISON. It is still possible to obtain our test in the UK, that is correct.

The CHAIRMAN. Have your sales declined with them?

Ms. GILL-GARRISON. Excuse me?

The CHAIRMAN. Have your sales in Britain declined as a result of your moving?

Ms. GILL-GARRISON. Have they declined——

The CHAIRMAN. I mean, the consumer complaints and the investigation of the British government.

Ms. GILL-GARRISON. We did not have consumer complaints. We were part of a campaign by an anti-genetic campaign organization, but we did not actually have consumer complaints. We have a data base of all of the actual inquiries, comments that we did obtain from consumers at that time. We are not actively marketing in the UK, so the most accurate answer to your question is, yes, sales have declined. We do not have an active marketing presence in the United Kingdom.

The CHAIRMAN. You disclaim testing for predisposition for disease, is that correct?

Ms. GILL-GARRISON. That is correct.

The CHAIRMAN. But the test results tell consumers that they have an increased risk of developing type 2 diabetes, high blood pressure and heart disease.

Ms. GILL-GARRISON. We actually have supplied a copy of the test to the group assembled here so that you can see the language that we do produce. We stop where the science stops. So there are very clear gene-diet interactions that focus on particular variations that are related to elevated homocysteine levels, for instance, elevated cholesterol levels. That is where our information particularly related to the genetic variations and the dietary interventions that we recommend is focused.

The CHAIRMAN. I hope you can understand why I am having a problem because I understand you disclaim testing for predisposition for disease. I have got somebody's report right here from your company and you are saying right here, "You may be at an increased risk of developing type 2 diabetes, high blood pressure and heart disease." That tells me that it is a pretty scary diagnosis.

Ms. GILL-GARRISON. Indeed. I would like to see the actual part of the report that that came from and I would also like to have an opportunity to address the finding of the GAO so that we can clarify that. The 14 different results that were found are not surprising to me because there were 14 different lifestyle questionnaires.

If you look through the report example that you have there, you will see that we provide personalized information to the individual based on their questionnaire results, and this is a way of telling people how they are doing in particular nutrition areas. There is

quite a lot of research that has been done that demonstrates that consumers really don't have a good feeling for their actual nutrient intake, and so our lifestyle questionnaire is designed to give them feedback on what their vitamin B intake is, for instance, and then we set goals which are based on the genetics. Also, as you go through the report, you will find sections that describe the activity of the different genes, the biomarkers such as cholesterol levels, homocysteine levels that can be affected by these variations.

The CHAIRMAN. Well, now Mr. Coleman is saying that your questionnaire doesn't even ask if your people are on medication.

Ms. GILL-GARRISON. We do on the report recommend that anyone that is on the medication or under the care of a physician seek out the advice of that physician before taking on any of the information that we provide in these reports.

The CHAIRMAN. But you don't ask them what their medications are?

Ms. GILL-GARRISON. Not at this time.

The CHAIRMAN. Would it be a good idea?

Ms. GILL-GARRISON. That is an interesting question. It is something that we are exploring with our ethics advisers at this point.

The CHAIRMAN. Just last week, the NIH issued a statement about genetic testing for type 2 diabetes and they say, "While the genetic variant does predict a greater risk of developing type 2 diabetes, the researchers are not recommending routine genetic testing for it. We don't currently have evidence that such a test would mean better outcomes for patients or that it would be cost-effective."

I guess in light of that, I wonder, is your company going to discontinue offering type 2 diabetes testing.

Ms. GILL-GARRISON. We don't offer type 2 diabetes testing. We look at particular genetic variants that are related to insulin sensitivity, and I think that what you can find in the scientific literature is some discordance in what is an agreeable end point for a person's health care. Do we think that monitoring cholesterol levels, keeping cholesterol levels low, is an adequate end point, or do we have to wait to see whether or not they go on to develop full-blown heart disease, full-blown cancer, before we can intervene with nutritional advice and information?

The CHAIRMAN. Thank you all for coming. This may not have been pleasant, but I think it is very, very important that we not exploit and mislead people. There is a lot of doom and gloom that comes with the findings that come out of your companies and your labs. I don't want consumers preyed upon in such a manner. I don't want costly, potentially harmful supplements to be sold to people without a full medical involvement as it relates to genetic testing and I think we have to do a better job of protecting privacy. So we are going to lean on the Government with the next panel.

We cast no personal aspersions on you. We have great concern about this industry. We want to see the promise of the Genome Project fully realized, but this industry, I fear, is getting ahead of that and may be doing damage to customers in a way that will set us back. I don't think you want that, I don't want that, and the American people deserve better than that. So with that, we will thank you and dismiss this panel and call up our third.

On our final panel, we will hear from Thomas Hamilton, who is the director of the Survey and Certification Group at the Centers for Medicare and Medicaid Services, and Dr. Steve Gutman, director of the Office of In Vitro Diagnostic Devices at the Food and Drug Administration.

Gentlemen, to be consistent with the other panels, would you stand and be sworn?

Do you promise that the testimony you are about to give will be the truth, the whole truth and nothing but the truth, so help you God?

Dr. GUTMAN. I do.

Mr. HAMILTON. I do.

The CHAIRMAN. Thank you.

Steve, why don't we start with you?

STATEMENT OF STEVEN R. GUTMAN, M.D., DIRECTOR, OFFICE OF IN VITRO DIAGNOSTIC DEVICE EVALUATION AND SAFETY, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, ROCKVILLE, MD

Dr. GUTMAN. Good morning, Mr. Chairman and members of the Committee. I am Steve Gutman, director of the Office of In Vitro Diagnostic Device Evaluation and Safety within the Center for Devices and Radiological Health at the FDA.

The safety and quality of in vitro diagnostics, or IVDs, is of utmost importance to the agency and I appreciate the opportunity to discuss these devices and the findings of the GAO investigation. I have submitted testimony for the record. For my opening statement, I will provide a brief overview of our regulatory authority regarding IVDs.

The regulation of IVDs by FDA, like the regulation of all medical devices, is risk-based, with devices classified into different categories—class I, II or III. The FDA regulatory program is comprehensive and includes requirements for registration and listing of products for high-quality production using good manufacturing practices and for post-market reporting of adverse events. For some class I, most class II and all class III devices, FDA review is required before a new medical device can enter the marketplace.

FDA applauds the GAO for its work in investigating the important issue of genetic tests sold directly to the consumer. In the early stages of GAO's investigation, we briefed staff on the existing regulatory framework for devices generally and IVD products, in particular. As defined by law, a product is a medical device if it is intended for diagnosis of disease or other conditions, or for use in the cure, mitigation, treatment or prevention of disease. To the extent the tests GAO investigated make such claims, they are devices subject to FDA jurisdiction.

The next question we ask is what type of devices these are. If they are test kits or systems that are intended to be used at multiple laboratories, they are subject to FDA pre-market review. If the laboratories develop the tests themselves using commercially available active ingredients, then FDA regulations require that the tests be ordered by a physician or other person authorized under State law to order such tests.

The CHAIRMAN. Dr. Gutman, after having heard today what you did, shouldn't they all be under that basis?

Dr. GUTMAN. Well, it would depend on the State law, actually, so I can't actually——

The CHAIRMAN. But you don't have the jurisdiction to do that?

Dr. GUTMAN. Not to trump State law.

The CHAIRMAN. OK.

Dr. GUTMAN. These tests must be performed in laboratories that are certified by CMS as high-complexity under CLIA 1988.

At this point, Mr. Chairman, we are working to determine if some tests investigated were subject or are subject to pre-market review or other regulatory requirements. We have contacted the companies involved to gather information about the tests and will consider appropriate enforcement actions.

Having reviewed the information gathered by GAO, FDA experts have a number of scientific concerns, concerns you have clearly put on the table this morning, with these testing services and the diagnostic claims that they make. FDA believes that the tests being offered are not grounded in valid scientific evidence, and we agree with GAO that they largely appear both medically unproven and meaningless.

The agency looks forward to working with Federal partners to address concerns about Internet sale of genetic tests direct to consumers. We are active participants in the evaluation of genomic applications and practice and prevention program, which is spearheaded by CDC to perform technology assessment on specific tests, including direct-to-consumer testing. We have participated broadly in outreach programs with work groups at the NIH, and most recently we have participated in two working groups recommended by the Secretary's Advisory Committee on Genetics, Health and Society to address the specific issues on the table today of direct-to-consumer sale of genetic tests.

An important work item, as you have already noticed from one of these, is a collaborative development with FTC and CDC of an advisory alerting consumers to the hazard of direct-to-consumer genetic tests. This advisory cautions consumers on the importance of using trained health care professionals or genetic counselors before obtaining or acting on these tests.

We appreciate the efforts by the Committee and the GAO to examine the tests under discussion. We are committed to working with other Federal regulatory and non-regulatory partners to address the problems identified. Thank you for this time and I am happy to answer any questions you may have.

The CHAIRMAN. Doctor, do you think that the FDA should have jurisdiction to regulate home-brew tests? I just heard you, I think, agree with the GAO that these tests are not scientifically sound. Do you think you ought to have the congressional authority, the statutory authority?

Dr. GUTMAN. Yes, sir, I do believe we should. I actually believe we do.

[The prepared statement of Dr. Gutman follows:]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

STATEMENT OF

STEVEN GUTMAN, M.D., DIRECTOR

OFFICE OF IN VITRO DIAGNOSTIC DEVICE EVALUATION AND SAFETY
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH
FOOD AND DRUG ADMINISTRATION
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SPECIAL COMMITTEE ON AGING
UNITED STATES SENATE

JULY 27, 2006

FOR RELEASE ONLY UPON DELIVERY

INTRODUCTION

Mr. Chairman and Members of the Committee, I am Dr. Steve Gutman, Director, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD), Center for Devices and Radiological Health (CDRH) at the Food and Drug Administration (FDA or the Agency). I am a board certified pathologist. Before joining FDA, I had 15 years of practice experience running clinical laboratories of all sizes. For the past 14 years I have worked as an FDA regulator in the area of laboratory tests (referred to by FDA as in vitro diagnostic devices [IVDs]). As the Director of the Office of In Vitro Device Evaluation and Safety, I consider the safety and quality of IVDs to be of utmost importance and appreciate your invitation and the opportunity to discuss the findings of the General Accountability Office's (GAO) investigation of certain direct-to-consumer IVD tests.

REGULATORY OVERVIEW

The regulation of IVDs by FDA, like the regulation of all medical devices is risk-based, with devices classified into low-risk (class I), moderate-risk (class II), or high-risk (class III) categories. The FDA regulatory program is comprehensive and includes requirements for registration and listing of products, for high-quality production using good manufacturing practices, and for post-market reporting of adverse events. For some class I, most class II, and all class III devices, FDA review is required before a new medical device can enter the marketplace.

GAO'S INVESTIGATION

FDA applauds the GAO for its work in investigating the important issue of genetic tests sold directly to the consumer. In the early stages of GAO's investigation, we briefed GAO staff on the existing regulatory framework for devices generally and IVD products, in particular. A product is a medical device if it is intended for diagnosis of disease or other conditions, or for use in the cure, mitigation, treatment, or prevention of disease. To the extent the tests GAO investigated make such claims; they are devices subject to FDA jurisdiction.

The next question is what type of devices these are. If they are test kits or systems that are intended to be used at multiple laboratories, they are subject to FDA pre-market review. If the laboratories develop the tests themselves using commercially available active ingredients, then FDA regulations require that the tests be ordered by a physician or other person authorized under state law to order such tests, and that they be conducted in laboratories certified by the Centers for Medicare and Medicaid Services as high complexity under the Clinical Laboratory Improvement Amendments of 1988. If the test is not ordered by a physician or authorized person or the laboratories that conduct the tests are not certified as high complexity, then the tests would violate these restrictions.

MOVING FORWARD

At this point, we are working with GAO to determine if some tests investigated were subject to FDA pre-market review or other regulatory requirements. We have contacted the companies involved to gather information about the tests and will consider

appropriate enforcement actions. Having reviewed the information gathered by GAO, FDA experts have a number of scientific concerns with these testing services and the diagnostic claims that they make. FDA believes that the tests being offered are not grounded in valid scientific evidence. We agree with GAO that they largely appear both medically unproven and meaningless.

FDA looks forward to working with GAO and other federal partners to address concerns about internet sale of genetic tests directly to consumers. We are active participants in the Evaluation of Genomic Applications in Practice and Prevention program spear-headed by the Centers for Disease Control and Prevention (CDC) to perform technology assessment on specific tests, including direct-to-consumer testing. We have participated broadly in outreach programs with work groups at the National Institutes of Heath.

Most recently, we have participated in two working groups recommended by the Secretary' s Advisory Group on Genetics, Health, and Society to address the specific issues of direct–to-consumer sales of genetic tests. An important work item from one of the working groups has been the collaborative development with the Federal Trade Commission and CDC of an advisory alerting consumers to the hazards of direct–to-consumer genetic tests. This advisory cautions consumers on the importance of using trained health care professionals or genetic counselors before obtaining or acting on genetic test information.

CONCLUSION

FDA appreciates the Committee's and the GAO's efforts to examine the tests under discussion today. We are committed to working with other federal regulatory and non-regulatory partners to address the problems identified. Thank you again for the opportunity to testify today. I am happy to answer any questions you may have.

The CHAIRMAN. Mr. Hamilton.

STATEMENT OF THOMAS HAMILTON, DIRECTOR, SURVEY AND CERTIFICATION GROUP, CENTER FOR MEDICAID AND STATE OPERATIONS, CENTERS FOR MEDICARE AND MEDICAID SERVICES, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, WASHINGTON, DC

Mr. HAMILTON. Good morning, Chairman Smith. Thank you for the opportunity to come here today and discuss the manner in which CMS implements the Clinical Laboratory Improvement Amendments of 1988, otherwise known as CLIA.

CLIA established nationally uniform quality standards for all clinical laboratories and all their testing to ensure the accuracy, reliability and timeliness of patient test results, regardless of the setting in which the test was performed. Those requirements apply across the full spectrum of lab tests, including genetic tests.

Under CLIA, as Dr. Gutman explained, three categories of laboratory tests have been established—waived tests; tests of moderate complexity, including the sub-category of provider-performed microscopy; and tests of high complexity. CLIA specifies detailed quality standards for the latter two categories and most genetic tests fall into the high-complexity category.

To enroll in the CLIA program, laboratories must register by completing an application, pay fees, be surveyed if they perform tests of moderate or high complexity, and receive a CLIA certificate. Laboratories that perform moderate and/or high-complexity tests must be surveyed onsite biennially in order to maintain certification, and may choose whether they wish to be surveyed by CMS or CMS's agent or by a private CMS-approved accrediting organization. Laboratories that conduct only waived or provider-performed microscopy tests are subject to surveys only if a complaint is alleged.

The CMS survey process focuses on outcomes; that is, we focus on the test results and the actual or potential harm that may be caused to patients due to inaccurate testing. Education and enforcement are both used. An educational approach permits a surveyor to provide resources and an explanation of the applicable requirements to the laboratory. This facilitates the laboratory's ability to correct deficiencies prior to imposition of enforcement actions.

However, if the laboratory cannot or will not correct the problems within a reasonable and specified amount of time, sanctions are imposed that are commensurate with the history, seriousness and pervasiveness of the deficiencies. Fulfillment and enforcement of CLIA standards is CMS' primary focus.

When CMS finds problems during a survey, the laboratory is generally provided an opportunity to correct those problems prior to enforcement actions, unless there is actual or potential harm to patient safety or there are recurring deficiencies. Over the past 5 years, CMS has initiated enforcement action in more than 5,000 cases. These proposed sanctions carry a clear communication: problems must be fixed promptly and effectively. I am pleased to say that in less than 8 percent of the time that we proposed such sanctions have we actually needed to implement the sanctions because of laboratory failure to take effective and timely remedial action.

I wish to emphasize that the Clinical Laboratory Improvement Amendments enacted by Congress and faithfully implemented by CMS have substantially improved the reliability and accuracy of laboratory testing in this country. The first onsite surveys of laboratories conducted right after CLIA implementation in 1992, for example, revealed that up to 35 percent of laboratories had significant quality control and quality assurance problems. Currently, less than 7 percent of the labs surveyed by CMS each year have such quality control or quality assurance problems.

More recently, the percentage of laboratories that meet our proficiency testing standards has increased from about 88 percent in 1988 to about 93 percent in 2003. We place high importance on strengthening the application of CLIA requirements for genetics testing and for all laboratory testing. To such an end, for example, in 2003 we strengthened quality control standards. In 2004, we established performance standards for State agencies. Also, in 2004 we initiated national meetings with all accrediting organizations to strengthen the national system and enter into better information-sharing agreements.

In 2005, we implemented national cytology proficiency testing for all people who examine pap smears. For the first time, more than 12,000 people took individual exams to test their individual ability to make accurate readings of pap smears. In 2006, we implemented a national electronic tracking system for all complaints and all complaint investigations received by CMS and State survey agencies.

It is important to note that the laboratories conducting genetic tests are already subject to existing CLIA regulations. Tests for genetic markers are dispersed throughout the various specialties identified in the regulations, and requirements for those tests are encompassed by the current quality standards.

In addition, we strengthened the CLIA regulations in 2003 and incorporated certain recommendations related to genetic testing that came from the Secretary's Clinical Laboratory Improvement Advisory Committee, otherwise known as CLIAC. Examples include additional confidentiality requirements, facility work flow requirements to minimize contamination, and quality control requirements for the genetic test method of polymerase chain reaction.

When problems are identified with any laboratory, including laboratories that conduct genetic tests, we take action. For example, earlier this month we issued a notice of potential revocation of the CLIA certificate for one laboratory conducting genetic tests and we are currently in the process of conducting a complaint investigation for a number of other laboratories that reportedly conduct genetic testing.

Our reconnaissance periodically identifies a few laboratories that we believe should have registered under CLIA, but which have not done so, or laboratories that have a CLIA certificate, but have expanded their testing beyond the areas for which they are certified. In such cases, we communicate with the laboratory and subsequently take enforcement action if we do not receive a favorable and timely reply. Such enforcement action may include revocation of the laboratory's CLIA certificate, if it already has a certificate,

or an injunction to cease testing if the laboratory does not have a CLIA certificate.

In conclusion, we in CMS are dedicated to ensuring the accuracy of test results from our Nation's laboratories, including those conducting genetic tests. There is no substitute for objective, trained personnel examining the quality of health care onsite. That is the purpose of the survey and certification system.

I thank the Committee and you personally, Chairman Smith, for your interest in improving clinical laboratory testing in the United States and I look forward to answering any questions you may have about our efforts.

[The prepared statement of Mr. Hamilton follows:]

TESTIMONY OF

THOMAS HAMILTON

DIRECTOR

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CENTER FOR MEDICAID AND STATE OPERATIONS

CENTERS FOR MEDICARE & MEDICAID SERVICES

ON

CLIA AND GENETIC TESTING

BEFORE THE

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July 27, 2006

CMS

CENTERS for MEDICARE & MEDICAID SERVICES

TESTIMONY OF
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Chairman Smith, Senator Kohl, distinguished members of the Committee; I thank you for your invitation to appear before the Committee. This morning I will address CMS' efforts to ensure quality results in our nation's labs, including those conducting genetic tests. To accomplish that task, the Centers for Medicare & Medicaid Services (CMS) works with a number of different entities, including state government agencies, professional associations and independent survey groups, to ensure that laboratories receiving Medicare payments comply with established conditions of participation for their provider type and that all laboratories in the U.S. meet standards established under the Clinical Laboratory Improvement Amendments (CLIA).

CLIA Background

In 1988, Congressional hearings concerning deaths of women from erroneously read Pap smears, and the proliferation of bench top laboratory technology into non-traditional testing sites, led to passage of CLIA. CLIA established nationally uniform quality standards for all clinical laboratory testing to ensure the accuracy, reliability and timeliness of patient test results regardless of the setting in which the test was performed. A laboratory subject to CLIA is defined as any facility that performs laboratory testing on specimens derived from humans for the purpose of providing information for the diagnosis, prevention, or treatment of a disease or impairment, or to assess the patient's health. CLIA is user fee funded; therefore, all costs of administering the program must be covered by the regulated facilities, including certificate and survey costs.

Final CLIA regulations were published on February 28, 1992 and are based (as required by statute) on the complexity of the test method; thus, the more complicated the test, the more stringent the compliance and oversight requirements. Three categories of tests have been established: waived; moderate complexity, including the subcategory of provider-performed microscopy (PPM); and high complexity. Laboratories performing only waived tests must enroll in CLIA, pay the applicable fee and follow manufacturers' testing instructions. Laboratories that perform moderate and high complexity tests are assessed additional certificate and survey fees based on their testing volumes and scope of testing. It is important to note that CLIA's application is to the methods used by the laboratories to conduct the various tests and not the effectiveness of the tests themselves. That latter point is an area of FDA authority.

Most genetic tests fall into the high complexity category. High complexity tests require more training and education, are more technique-dependent, (more complicated to perform and have more steps), and require interpretation of the results. They are therefore subject to the most stringent standards and are reviewed during laboratory surveys. CLIA also specifies detailed quality standards for moderate complexity tests.

There are a number of tests that do not fall under CLIA and laboratories or entities that perform them do not have to adhere to CLIA standards insofar as they are only performing these particular tests. They include:

- parentage testing;
- breath-a-lizer tests used by law enforcement to determine intoxication, and all other breath testing;
- drugs of abuse tests performed by SAMHSA (Substance Abuse and Mental Health Services Agency) certified laboratories;
- any clinical laboratory testing used in research, the results of which are not reported to a caregiver or to the patient and are not used in any way to treat or medically evaluate a patient for treatment;
- in-vitro vertilization testing prior to implantation;
- slit lamp testing;
- genetic tests that don't provide information related to health assessment, diagnosis, monitoring or treatment;
- forensic testing;
- tests in which a specimen is not removed from the body; and
- employee drug testing for the purpose of employment.

CMS is charged with the implementation of CLIA, including laboratory registration, fee collection, surveys, surveyor guidelines and training, enforcement, and approving entities that test laboratory proficiency, accrediting organizations, and exempt states with equivalent requirements. The Centers for Disease Control and Prevention (CDC) is responsible for CLIA research studies, convening the Secretary's Clinical Laboratory Improvement Advisory Committee (CLIAC) and providing scientific and technical support/consultation to DHHS/CMS. The Food and Drug Administration (FDA) is responsible for test categorization.

Laboratory Enrollment and Performance Standards

To enroll in the CLIA program, laboratories must register by completing an application, paying fees, and undergoing an inspection survey, if applicable, prior to receiving a CLIA certificate. Currently there are 195,000 laboratories enrolled in CLIA and it is estimated that approximately 2,000-2,400 laboratories perform genetic tests. CLIA fees are based on the type of certificate requested by the laboratory (that is, waived, provider performed microscopy (PPM), accreditation, or compliance), as well as the annual volume and types of testing performed for moderate and high complexity laboratories. Waived and PPM laboratories may apply directly for a certificate and are not subject to routine inspection, unless a complaint is registered. Laboratories that must be surveyed routinely (i.e., those performing moderate and/or high complexity testing—including genetic tests) may select between CMS and a private accrediting organization to fulfill that requirement.

The biennial CMS survey process is outcome (test result) oriented and utilizes a quality assurance focus to assess compliance. An educational approach is employed in which the surveyor may provide resources and an explanation of the requirements to help the laboratory correct deficiencies and comply with applicable standards in order to avoid enforcement actions. However, if the laboratory cannot correct the problem(s) within a reasonable amount of time, sanctions are imposed that are commensurate with the history, seriousness and pervasiveness of the deficiencies.

Laboratories subject to routine biennial surveys must comply with a number of CLIA quality requirements, including:

- Personnel: CLIA sets minimum qualifications, experience and training requirements for all persons performing or supervising moderate or high complexity tests. These individuals must also meet specific responsibilities that correspond to all of the CLIA quality standards.
- Proficiency testing: Laboratories must also participate in an approved proficiency testing program that provides an external evaluation of the accuracy of the lab's test results. Under this requirement, three times per year, laboratories purchase samples from an external source (the proficiency testing provider), whose characteristics are not disclosed to the lab. The laboratory tests the samples along with their routine patient testing and the results are returned to the testing provider to be graded. If the laboratory passes, they have met the CLIA standard. The results of proficiency testing for all laboratories in CLIA are transmitted to CMS and are routinely monitored and maintained in a database. If a laboratory repeatedly fails proficiency testing during successive testing challenges, then action is taken to limit the laboratory's ability to continue performing the test(s). Proficiency testing providers are private companies, or state laboratory departments, that must meet certain CLIA requirements to provide testing samples to labs, and are approved by CMS annually. There is no proficiency testing material available for most genetic tests. Therefore, CLIA provides an alternative mechanism to ensure accuracy: twice per year, the laboratory must perform a study to verify the accuracy of their tests. Many laboratories utilize an inter-laboratory comparison of the results of the same specimen to meet this requirement.
- Quality control (QC): Laboratories must have a process for monitoring personnel, and testing equipment and the lab's environment to ensure proper operation and accurate results each day. QC also includes verifying, or in the case of most genetic tests, establishing the analytical validity of the test to ensure that the test works correctly in this laboratory.

- Quality assessment: Laboratories must have and follow a plan to monitor, on an ongoing basis, the overall operation of the laboratory, provide communications, and resolve problems that affect the quality of their testing.
- Cytology testing: CLIA sets special rules for cytology testing including workload limits, individualized proficiency testing, personnel standards, and quality control.
- The laboratory must maintain a recordkeeping system for the entire testing process.

Data show that these regulations are helping to improve testing quality. Since CLIA was implemented in 1992, quality deficiencies cited against clinical laboratories have decreased significantly. The first on-site surveys of laboratories revealed that up to 35 percent of laboratories had quality deficiencies. Currently less than 7 percent of 11,000 laboratories surveyed by CMS in a year have quality problems. We believe that our educational rather than punitive approach has facilitated improvement in laboratory quality. Data from our Survey Evaluation Form indicate that most laboratories respond very positively to the educational, information-sharing approach to oversight, and correct their problems prior to imposition of enforcement actions. The quality assurance approach encourages laboratories to develop a plan to monitor their entire operation to identify and resolve their quality-related problems on an ongoing basis. Survey data and proficiency testing data reflect improvement in laboratory performance over time, thus demonstrating labs' accountability in knowing the regulatory requirements and preventing and correcting identified issues. Over the past five years, CMS has proposed enforcement action in 5,361 cases, and carried out such action in 395 instances.

Oversight and Surveys

CMS contracts with State Departments of Health to perform laboratory surveys. CMS' objective in developing an outcome oriented survey process is primarily to determine the laboratory's regulatory compliance, but also to assist laboratories in improving patient care by emphasizing those aspects that have a direct impact on the laboratory's overall test performance. CMS promotes the use of an educational survey process. The surveyor determines, based on observation of the laboratory's (past and current) practices, interviews with the laboratory's personnel and review of the laboratory's relevant documented records, whether the laboratory is meeting the requirements of the CLIA regulations to produce accurate, reliable and timely

(quality) test results. The surveyor meets the objectives by employing an outcome-oriented/quality improvement type of survey process or approach, the intent of which is to focus the surveyor on the overall performance of the laboratory regarding the applicable standards and the way it monitors itself, rather than on a methodical evaluation of every standard level regulatory requirement.

The quality assessment (QA) requirements of the laboratory regulations (42 CFR Part 493, Subpart K) guide the surveyors in organizing their review. The surveyors select a cross-section of information, tour the facility and observe the entire testing process, interview staff and management, review quality records and all aspects of the laboratory's operation to assess its capability to produce quality results as well as its ability to identify and correct problems and communicate with its clients. Emphasis is placed on overall laboratory performance and the structures and processes contributing to the reliability of the testing. Since it would be impossible to review every test and every document in the laboratory, the surveyor reviews the selected cross-section of information to see if the laboratory has established and implemented appropriate mechanisms for monitoring and evaluating its practices and solving its problems. The surveyors investigate further any test areas identified as a problem but not addressed by the laboratory's QA program, ensure permanent resolution of previous deficiencies and review any new tests and personnel since the last visit. If the laboratory is failing to monitor (or effectively monitor) its own systems, the surveyor may direct the laboratory to the requirements and the relevant regulatory sections for its particular setting, thereby accomplishing the educational aspect of the survey process.

If, however, problems identified during the survey, or as the result of a complaint, are not remedied in a reasonable amount of time, CMS has authority to impose a variety of sanctions on the laboratory. These range from onsite monitoring, fines, or loss of Medicare reimbursement, to revocation of their CLIA certificate, depending on the seriousness and pervasiveness of the problem. Most laboratories correct their problems as a result of the education they receive during and following the survey, and no sanctions are imposed. Only about one percent of laboratories surveyed each year have had enforcement actions taken against them. The names of these laboratories and the laboratory director are compiled annually and this list is placed on the

CLIA web site at: www.cms.hhs.gov/clia. The 2005 registry lists 240 entities. The percentages of each laboratory type experiencing enforcement actions are proportional to the total number of laboratories of that type enrolled in the CLIA program. Laboratories with repeat deficiencies are treated more aggressively with progressively severe expedited enforcement actions.

As mentioned previously, laboratories that are subject to biennial surveys can choose to obtain CLIA certification by the State agency, as an agent of CMS, or by an approved private accreditation organization. Accrediting organizations with standards that are equivalent to or more stringent than CLIA, currently approved by HHS for this purpose include:

- the Joint Commission on Accreditation of Healthcare Organizations (JCAHO);
- the College of American Pathologists (CAP),
- COLA (formerly Commission on Office Laboratory Accreditation);
- AABB (formerly the American Association of Blood Banks);
- the American Society for Histocompatibility and Immunogenetics (ASHI); and
- the American Osteopathic Association (AOA).

States that have laboratory licensure program standards equivalent to, or stricter than those of CLIA can apply for "approval" or "exemption." Then the laboratories in those states that meet state licensure requirements are deemed to be in compliance with CLIA. There are currently only two exempt states – New York and Washington. In other states that have a state laboratory licensure program, laboratories within the state must comply with both CLIA and their state requirements.

On an annual basis, CMS, through the state agencies, surveys approximately 2.5 percent of accredited and exempt laboratories using CLIA standards to validate that these laboratories are in compliance with CLIA by meeting the accrediting organization's standards and to ensure that the organization is enforcing its own equivalent standards. After surveying the accrediting organization's laboratories, CMS compares the results of the state survey to the accrediting organization's, to determine the level of disparity. The rate of disparity is the percentage of all sample validation surveys for which a State survey agency finds non-compliance with one or

more CLIA conditions when no comparable condition level deficiency was cited by the accreditation organization. As set forth in regulation at 42 CFR 493 Subpart E, an accreditation program with a disparity rate of 20 percent or more is subject to a review to determine if that organization has adopted and maintains requirements comparable to those of CMS. No accrediting organization has even approached the maximum threshold of 20 percent disparity.

Complaints alleged against accredited laboratories from any source are either addressed by the accrediting organization or by the State agency in conjunction with the CMS Regional Office. CMS has recently implemented an automated complaint tracking system to capture all complaints to ensure timely and complete follow up and investigation. Ultimately the approved accrediting organizations and exempt States will enter their complaint data into this system to provide national data for CMS to monitor for program effectiveness.

It is important to note at this point that genetic testing is already covered by existing CLIA regulations. Tests for genetic markers are dispersed throughout various laboratory specialties and the requirements for those tests are encompassed by the current quality standards. In fact, the final CLIA Quality Control regulation that was published in 2003 incorporated certain CLIAC recommendations for genetic testing, including confidentiality requirements, facility workflow requirements to minimize contamination, and quality control requirements for the genetic test method of polymerase chain reaction (PCR). When problems are discovered with any lab, including laboratories conducting genetic tests, we take action. For example, earlier this month the in its capacity as CMS' CLIA survey agent, the State Survey Agency in Connecticut sent a letter to Genaissance Pharmaceuticals informing them that the "nutrigenomic" tests they were conducting are subject to the requirements of CLIA and that they are, therefore, required to supply documentation of their test method validation studies for such tests. Subsequently, the laboratory has agreed to permit an inspection of these tests.

Conclusion

CMS takes its responsibility to ensure the quality of laboratory tests, including genetic tests, seriously and we will continue to do so. I thank the Subcommittee for its time this morning and would be pleased to answer any questions you might have.

The CHAIRMAN. Thank you, gentlemen. No doubt, you individually and your agencies are doing much good work, but we have got a problem. I think this hearing has made that abundantly clear to me; I hope it has to you. Here we sit, 6 years after discussions about genetic testing under CLIA, but we don't have a rule in place. So I am wondering why, over the last 6 years, we don't have a stronger regulatory process for them.

Mr. HAMILTON. We did promulgate additional rules in 2003 that strengthened the quality control processes and we drew upon the CLIAC committee recommendations quite heavily in doing so. We continue to evaluate the need for additional rules, but we do believe at this point that the greatest gain can be made in strengthening our application of existing rules and adopting as comprehensive an approach as possible.

Let me try to put the situation into context. It may be useful to think about this entire situation in terms of five different activities: the advertising of genetic tests, the sale of genetic tests, the testing itself, the interpretation of results, and the communication of those results to consumers. Of those five, CLIA focuses on the testing itself, and within testing, CLIA focuses not on clinical validity, not on the question of whether the test is of value to the consumer and measures the right things, but rather the analytical validity. Does the measurement process measure what it is supposed to be measuring.

The CHAIRMAN. So you don't speak at all as CMS, anyway, to ensure the accuracy, utility and safety and validity of the home genetic tests themselves?

Mr. HAMILTON. CLIA speaks to the analytical validity. Are the tests done accurately and reliably? But that additional regulation for CLIA itself——

The CHAIRMAN. You evaluate the process, but their conclusions, you don't evaluate their legitimacy?

Mr. HAMILTON. There would be nothing to prevent a company from taking these and over-claiming through hyperbolic claims about effectiveness or extending the results in a consumer sales process. I think it was Dr. Hudson who emphasized the need for a fairly comprehensive approach, and that is why we are engaged with CDC and the FTC in looking at all of this because it all has to work together. Our particular job in CLIA is really to make sure that the testing itself is accurate and reliable.

The CHAIRMAN. Have you looked at any of their websites and found hyperbolic claims?

Mr. HAMILTON. Indeed, and we are very concerned about that. I found hyperbolic claims. I found the kinds of statements that are so vague and apply to so many people that it might amount to no more than a genetic horoscope.

The CHAIRMAN. Do you think they have any liability for such a thing?

Mr. HAMILTON. I think that is a consumer sales and protection realm of activity and I can speak only to the question of CLIA itself.

The CHAIRMAN. If they do have erroneous results, if you were in their place, you would be concerned about liability.

Mr. HAMILTON. To the extent that a laboratory is performing genetic tests that are subject to CLIA and does note have a CLIA certificate, they have a liability. To the extent that they are performing tests inaccurately, then we not only have a concern, but the laboratory ought to have a real concern about those results.

The CHAIRMAN. Do you have any concerns about privacy of the people, of their customers?

Mr. HAMILTON. Protecting privacy is an important part of the CLIA regulations, as well as the Privacy Act on Health Insurance Portability and Accountability Act (HIPAA). Both of those are invoked under the CLIA regulation. We have heard a number of instances in which laboratories seem to be doing testing, but do not have a CLIA certificate and have not registered for one. In our reconnaissance of those, we are following up with such laboratories and informing them of the need to make such application, and to the extent that they refuse to do so, then we follow up either by removal of any existing CLIA certificate or by an injunction to cease testing.

The CHAIRMAN. Dr. Gutman, am I accurate that the evaluation of the clinical validity of the tests is the responsibility of your agency, of the FDA?

Dr. GUTMAN. Well, that certainly is one of the charges in the products that we review, yes.

The CHAIRMAN. What are you doing to protect consumers from fraudulent tests?

Dr. GUTMAN. Well, in general, for tests that we are reviewing, we, in fact, on a test-by-test basis look at the claim and do establish both analytical and clinical validity. As you probably know, sir, for many of these tests we have currently been applying enforcement discretion and approaching these on a risk-based basis. So we have taken some action.

We are assessing what our role might be. As Dr. Hudson suggested, this is a very complex and nuanced area and as we assess this, we would like to see regulatory controls put into place. We are very concerned that we not chill this technology, so we actively are addressing how to approach this.

The CHAIRMAN. Well, I just want to encourage stepping on the accelerator.

Dr. GUTMAN. OK. I appreciate that comment.

The CHAIRMAN. I think you see the promise in genetic testing. I hope you come away from this hearing with a suspicion that some damage is being done to that promise, and there may be marketing going on right now that is simply today's snake oil and we owe the American people better than that.

Thomas, specifically, are nutrigenomic tests subject to CLIA regulation?

Mr. HAMILTON. It depends on exactly what they are testing and the purpose of those. I think the kinds of examples that you have brought out in today's hearing—we would say they are subject to CLIA. We look first to ask whether or not they are using specimens from the human body. Yes. Are they providing information? Yes. Are they providing information for the purpose of diagnosing or treating or preventing disease or impairment, or for the assessment

of a person's health? If yes, if all those things pertain, they are subject to CLIA.

The CHAIRMAN. My understanding is all those are answered yes in the cases we have looked at.

Mr. HAMILTON. That is my interpretation, yes.

The CHAIRMAN. So I would certainly encourage a biomarker assessment or a regulation such as performed by Genox be subject to CLIA regulation. If it isn't now, I really do encourage that it be included.

How can a doctor or a patient find out whether a lab or CLIA-certified?

Mr. HAMILTON. They can go to our website and get information about the laboratories. I appreciate that sometimes navigating through our website is a difficult process, particularly since we just reorganized it. So that is an area that we are looking at in terms of how we can make information about laboratory status more effective.

The CHAIRMAN. Is it a concern to CMS if a lab represented itself as CLIA-certified but is not?

Mr. HAMILTON. It is of great concern to us if a lab represents itself as certified.

The CHAIRMAN. Well, I would strongly encourage that the website be made easier, user-friendly, and that these kinds of representations be pursued by CMS.

Mr. HAMILTON. I think one of the things that is coming out from the GAO report that we have a deeper appreciation for is some of the claims made by companies and some of the confusion that may be out there as to whether or not some of these laboratories do fall under CLIA. That is something that we can remedy, and we will be issuing additional communications to the field making it very clear that these laboratories are subject to CLIA.

The CHAIRMAN. Gentlemen, thank you for being here. Again, we appreciate your work. I did not know where this hearing was going to go when a year ago—or if we would even have a hearing—when I asked for this review. But looking at the review, I am alarmed, and the stewardship falls to your agencies to provide a framework that keeps the Genome Project promise, protects consumers and, frankly, stops perhaps industry practices which amount to fraud.

I am not concluding that, but I am suspicious of it, and this Committee is going to continue to encourage you. After 6 years, let's get the regulatory structures in place so that the American people are protected and the promise of genetic testing is not damaged by some who may take advantage of unsuspecting American consumers.

So thank you all, and we are adjourned.

[Whereupon, at 11:54 a.m., the Committee was adjourned.]

APPENDIX

PREPARED STATEMENT OF SENATOR KEN SALAZAR

Thank you Chairman Smith and Ranking Member Kohl for holding today's hearing.

Throughout its history, the Aging Committee has led the way in calling attention to important public policy issues impacting older Americans and has not been afraid to take on industries that prey on vulnerable seniors.

As Colorado's Attorney General, I spent considerable amount of time and energy protecting the elderly in my state from fraud and abuse. I consider the creation of the Medicaid Fraud Unit one of my proudest accomplishments.

I welcome the witnesses testifying here today. It is my hope that they can shed light on an industry that I have only recently learned existed: the Direct-to-Consumer Genetic Testing Industry. In particular, I thank Ms. Rosalynn Gill-Garrison, who is here representing Sciona Inc., headquartered in Boulder, Colorado.

Sciona has been bery cooperative throughout Aging Committee's investigation on the practices of companies currently engaged in Direct-to-Consumer Genetic Testing. I appreciate their cooperation.

While advances in the field of genetic science continue to open doors in the field of healthcare and improving the quality of life for many people, many questions about on this emerging science remain open for discussion and debate.

I know I have many questions.

For example, how are these companies marketing their products and services? What are the effects of their products on Americans who receive their "genetic health forecasts"? And finally, how reliable is the science these companies employ?

There are certainly ground-breaking possibilities that genetic testing and diagnosis could bring to the field of healthcare, but I believe the impact on those using these products must always be of paramount concern.

Today, someone sitting at home on their couch can go to the drug store or log onto the internet and purchase a mail-in genetic test that purports to tell them whether they are genetically prone to any number of medical conditions, including heart disease, breast cancer, and Alzheimer's.

When that person receives the results from these tests in the mail, without the counseling and interpretation of a specialized medical professional, the results of these genetic tests can be confusing, alarming, and easily misinterpreted.

I am very interested in learning more about the GAO's recent investigation on these genetic and am pleased to see that GAO representatives are on hand to answer questions about their study.

At first glance, I find GAO's conclusions very troubling. GAO claims that tests sold by the companies here today frequently mislead individuals by making claims that they are unable to substantiate.

By submitting volunteer samples to genetic testing companies, they established a disturbing scheme. After being informed that they are susceptible to a number of serious and possibly chronic diseases, companies market and sell costly supplements, medical supplies, and further tests, which are either unnecessary or based on questionable science, to vulnerable Americans.

We have provided the companies named in this study an opportunity to defend their company practices. I fully anticipate they will detail the practices they are taking to ensure that their services and the representations they make to their customers are honest and accurate.

If America's seniors are indeed being sold a bag of goods, I believe it is the responsibility of our government to regulate this industry and to protect consumers.

I look forward to hearing the testimony of today's experts from CMS and the FDA to explain what regulations and oversight are these Direct-to-Consumer genetic testing firms currently fall under. In particular, I am interested learning whether CMS and FDA believe they have the authority to regulate these firms under current law.

If the answer is no, it may be the case that the members of this Committee need to work together to rectify this.

Again, I thank the Committee for holding today's hearing.

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August 4, 2006

Senator Barbara Mikulski
404 Russell Building
Washington, DC 20510

Re: July 27, 2006 Hearing on Home DNA Testing
Senate Special Committee on Aging

Dear Senator Mikulski:

On behalf of Genox Corporation, we are writing to express our thanks for the concern and assistance of your staff in connection with the above referenced hearing. We think that Genox Corporation was unfairly treated by the issuance of a subpoena that forced Genox to miss a convention in Chicago critical to its support of academic and governmental research into the causes and processes of aging. As the attached correspondence also shows, the committee's investigative staff caused a significant disruption in Genox's support of important scientific research projects, such as the analytical services that Genox provides to researchers at the National Institutes of Health and Johns Hopkins University. This disruption could have been avoided had the staff afforded Genox the courtesy of addressing the "findings" of a GAO report prior to and apart from the hearing, which had nothing to do with Genox's primary mission. Genox does not now and never has done DNA testing. We hope that your office can exert its influence to help prevent further abuse by the investigative staff.

Sincerely,

David A. Holzworth

Cc: Dr. Ellen-Marie Whelan

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August 3, 2006

Senator Gordon Smith
Chairman, Special Committee on Aging
404 Russell Building
Washington, DC 20510

Re: July 27, 2006 Hearing

Dear Senator Smith:

We are submitting this letter on behalf of Genox Corporation to supplement the remarks of its President, Dr. Rama Rathnam and his responses to your questions at the July 27, 2006 Hearing entitled "At Home DNA Tests: Marketing Scam or Medical Breakthrough." As you may know, Genox had to cancel attendance at a major convention and business meeting to prepare for and attend the hearing. This placed an unusually heavy burden on the company, which has only three employees, especially because no substantive information was provided to Genox prior to the hearing as to the concerns of the Committee or the information that had been provided to the Committee by GAO.

At the hearing, Genox learned for the first time that GAO had submitted to Genox a synthetic urine sample for an 8-OHdG ELISA analysis. The Committee seemed to think that Genox should have detected that the urine sample was synthetic. Detection of fake urine samples is not the function of the 8-OHdG ELISA kit. If Genox were a drug testing laboratory or if Genox were undertaking analysis for clinical, diagnostic or treatment purposes such a test might be appropriate. However, Genox has never been a CLIA certified laboratory and has always provided its laboratory services on the express understanding that its reported results are for research purposes only.

The GAO also apparently testified that a cheek swab was submitted to Genox for testing. We believe that the GAO witness misspoke. Genox does not do DNA testing and did not analyze any cheek swab for GAO or anyone else. We respectfully request that the GAO witness either correct or clarify his testimony to avoid impugning Genox's reputation.

We also respectfully request that GAO and the Committee provide to Genox all data, notes and documents on which the GAO findings as to Genox activities are based. We believe that the reputation of Genox as a specialized laboratory dedicated to the support of basic research for the advancement of science based knowledge on the processes of aging may have been impugned, even though the

Senator Gordon Smith
August 3, 2006
Page 2

investigation was well-intended. We think it very important to set the record straight and also to have fair access to the basis for the statements that were made by the GAO witness, under oath, at the hearing.

The Committee also asked if Genox was aware of the form or method that Suracell employed to report Genox analysis results to individual clients. Genox was quite surprised to learn that Suracell was even reporting analysis results to individual clients. Genox sample kits are clearly labeled "For Research use only." In addition, all Genox reports contained the following language: **NOTE:** *This report is intended to be used solely as a research tool in the study of oxidative stress related diseases and aging. The Genox Corporation assumes no responsibility for the use of this report for diagnosis, treatment, cure, or prevention of any health-related condition."*

When Genox first began to provide services to Suracell, the company made it very clear that Genox was not CLIA certified and that it would be improper to use Genox reports for clinical, diagnostic or treatment purposes for individuals. Genox understood that Suracell was using the data for evaluating the efficacy of its products. We do not believe that individuals could access analysis reports on the Suracell website at the time that Genox first began to provide services to Suracell.

The Committee did not seem to be aware that Genox suspended services to Suracell and all other non-academic and non-governmental entities immediately upon learning that the Genox results may have been used, contrary to Genox's express restriction, for purposes that may not be exempt from CLIA. This action was reported to the Committee's investigative staff a week before the hearing. In addition, Genox also immediately contacted Maryland and U.S. governmental regulatory authorities to make sure that all of its activities are in compliance with or are exempt from CLIA. Based on the same information that was provided to the committee investigative staff, the relevant regulatory authorities promptly confirmed that Genox laboratory services to academic and governmental research institutions are exempt from CLIA certification as confirmed by the attached letter.

We respectfully request that these supplementary remarks be made a part of the record of the Hearing.

Sincerely,

David A. Holzworth

cc: Senator Gordon Smith, Chairman (Oregon)
Senator Richard Shelby (Alabama)
Senator Susan Collins (Maine)
Senator James Talent (Missouri)
Senator Elizabeth Dole (North Carolina)

Senator Mel Martinez (Florida)
Senator Larry Craig (Idaho)
Senator Rick Santorum (Pennsylvania)
Senator Conrad Burns (Montana)
Senator Lamar Alexander (Tennessee)
Senator Jim DeMint (South Carolina)
Senator Herb Kohl, Ranking Member (Wisconsin)
Senator Jim Jeffords (Vermont)
Senator Ron Wyden (Oregon)
Senator Blanche Lincoln (Arkansas)
Senator Evan Bayh (Indiana)
Senator Thomas Carper (Delaware)
Senator Bill Nelson (Florida)
Senator Hillary Clinton (New York)
Senator Ken Salazar (Colorado)
Senator Barbara Mikulski (Maryland)

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August 3, 2006

BY TELECOPY, E-MAIL AND U.S. MAIL

Ms. Kathleen Steed
Laboratory Licensing Division
Maryland Department of Health & Mental Hygiene
Office of Health Care Quality
Spring Grove Center – Bland Bryant Building
55 Wade Avenue
Catonsville, MD 21228-4663

Re: Genox Corporation
Compliance Warning Letter

Dear Ms. Steed:

This letter will acknowledge your voice-mail message left on my answering machine on August 2, 2006 in reference to the compliance warning letter dated July 21, 2006 to Genox Corporation and the submission on behalf of Genox by this law firm dated July 26, 2006.

We understand that the Licensing Division forwarded Genox's submission for review to the Centers for Medicare and Medicaid Services (CMS) that runs the CLIA certification program. Judy of CMS responded orally to your request for review indicating that the Genox submission was sufficient to show that Genox laboratory services to governmental and academic researchers which is not used for diagnosis, treatment or prevention of diseases for individuals is exempt from CLIA certification and that Genox had discontinued all other services to companies such as Suracell that may have been using Genox laboratory reports for non-exempt purposes.

Genox is taking immediate additional steps to assure that its services are not misused. These steps include a revision of its website and all marketing materials to include the following restriction:

ATTACHMENT

Ms. Kathleen Steed
August 3, 2006
Page 2

ANALYTIC REPORTS FOR RESEARCH USE ONLY

The use of individual assay reports generated by Genox Corporation is restricted to research use only. The provision of these reports to individuals or to treating physicians for the diagnosis, prevention, treatment and control of any human disease or impairment of, or the assessment of the health, nutritional, or medical condition of individuals is expressly prohibited by law. 42 U.S.C. § 263a (2006); 42 C.F.R. § 493.3 (2006); COMAR 10.10.01.02 (2006). ***Genox is not a CLIA certified laboratory.***

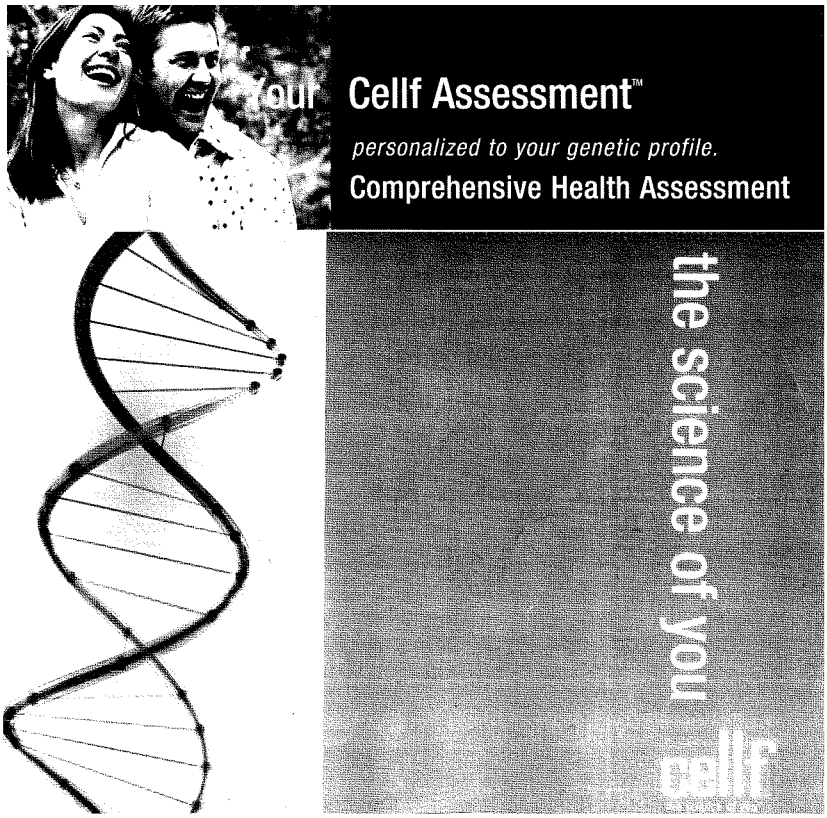
Genox is also meeting on August 7, 2006 with FDA officials to make absolutely certain that its laboratory services comply with all relevant regulations.

We wish to express appreciation on behalf of Genox for the professionalism, courtesy and promptness of your review, the CMS review and the expeditious resolution of this issue.

Very truly yours,

David A. Holzworth

cc: Rence B. Webster, OHCQ
Judy Yost, CMS CO


the science of you
Your Cellf Assessment™
personalized to your genetic profile.
Comprehensive Health Assessment

Jamie B. Sciona

We're pleased to be able to introduce you
to someone very unique–YOU!

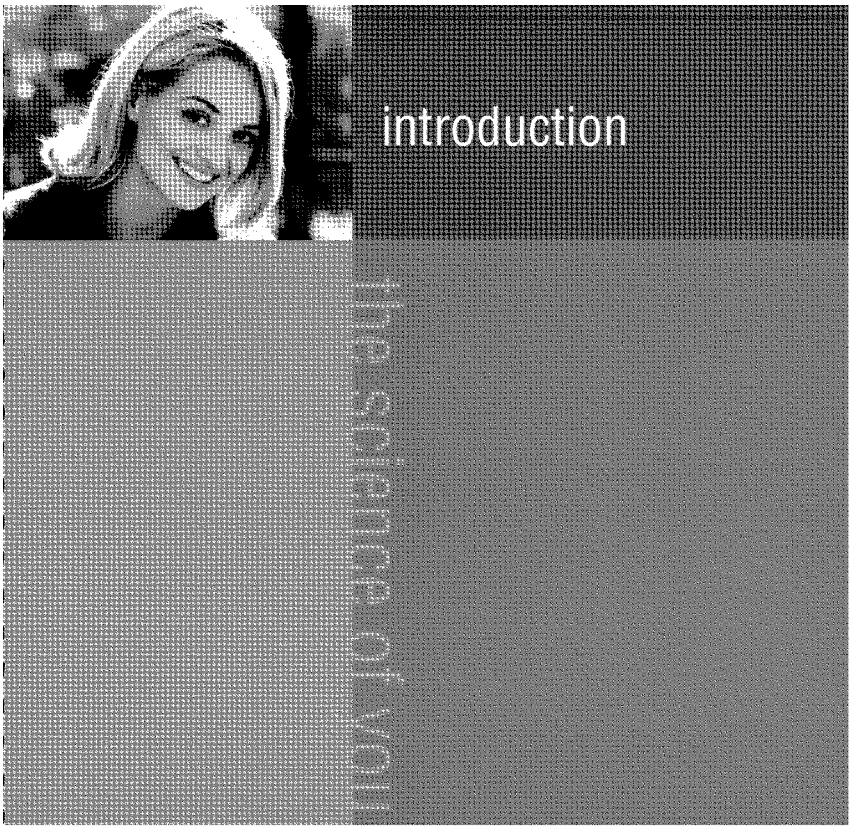
Welcome To Cellf™. The Science of You™.

This is the just the beginning of the journey to find out who you are, how your genes and your body work, and discover ways to optimize your health like never before. Your Cellf Assessment™ will provide you with health, nutrition, and lifestyle advice based upon your individual genetic profile and current lifestyle choices.

After reading your Cellf Assessment, you'll know if the choices you're making are the right ones for you. Your Cellf Assessment™ is completely personalized for you because Cellf recommendations are based on your own DNA. Small variations in your genes can influence how well your body metabolizes food, utilizes nutrients, and removes potentially damaging toxins; all of which can affect your short- and long-term health. By understanding how your unique genetic profile affects you, you can take charge of your own health and make informed decisions about your own diet and lifestyle options. This assessment will offer you specific advice, from the types and amounts of nutritional supplements to take to the kinds of foods to eat, that can create optimal wellness for you and you alone.

Of course, we know your privacy is extremely important to you. That's why, at all times, we ensure that the highest level of privacy and security of your personal information is maintained. The results of your report have been shared only with you.

So, let's get started. It's time to discover The Science of You!



introduction

the science of you

Table of Contents

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- Heart Health
- Inflammation
- Insulin Sensitivity
- Summary Table of Your Personalized Results for Your Healthcare Practitioner

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- Action Areas
- More Nutrition Facts
- Frequently Asked Questions
- Key Terms
- Population Frequency Chart
- Resource Directory

Understanding Genetics

Before reading your Cellf Assessment, please take a few minutes to review this background information that will help you better understand your results and enhance the overall value you receive from the important information contained in this personalized report.

What are Genes?

A gene is a segment of the DNA (short for deoxyribonucleic acid) molecule that contains the instructions for how, when, and where your body makes each of the many thousands of proteins required for life. Each gene is comprised of thousands of combinations of four letters that make up your genetic code: A, T, C, and G. These letters stand for the chemicals adenine, thymine, cytosine, and guanine. Each gene's code combines the "letters" A, T, C, and G in various ways, spelling out the "words" that specify which amino acid is needed at every step in the process of making the proteins required for your body to develop and function.

What Are Gene Variations?

With the exception of identical twins, all people have small differences in the information their DNA contains, and it's these differences that make each of us unique. Genes can come in different forms, commonly called variations which are slight changes in the genetic code that are present in at least one percent of the population. For example, one genetic "letter" (A, T, C, or G) may be replaced by another. These variations can lead to different processes in the body, just as altering one letter in a word can completely change its meaning; for instance, from "g"oat to "c"oat. When the variation affects only one genetic letter, as in the goat/coat example above, it is called a "single nucleotide polymorphism" (or SNP, pronounced "snip").

Are Gene Variations "Bad"?

For different groups of people, one form of a gene may be more common than another, so one gene variation may be more common than another. Historically, scientists have referred to the most common form of the gene as the "normal" form, and the less common form as the variant form. However, as research progresses, scientists have learned that some variations which are less common in one group of people are more common in other groups of people. The form that is most common in particular groups can give us clues into the history and environment of our ancestors – a genetic family tree. The reason that these variations are important to your health is that in some cases, the variations in a gene may lead to a change that can alter the activity of a gene. For some genes, this could lead to reduced efficiency of the enzyme produced by the gene; in other cases this could lead to too much of a particular enzyme being produced. Your report will identify whether or not you have a particular variation in the gene but please remember that this is simply describing the form of the gene that you have. The genetic tables contained in your Cellf Assessment will identify which of the genes in your own genetic profile could have an impact on your health. We also provide information for you on the percentage of the population that has the same form of a gene as you.

What is Nutrigenetics?

The Cellf Assessment is a nutrigenetics test. Nutrigenetics is the science of gene – diet interactions. We apply this science to help you understand the impact of your own genes in response to your dietary and lifestyle choices. Nutrigenetic testing is a method that allows us to identify your own unique genetic variations so that we can provide you with dietary and lifestyle recommendations that can empower you to take control of your own health and well-being.

How to Read Your Report

Each section of your assessment is formatted the same way for your convenience. There's a quick overview of the particular health category being discussed (Heart Health, Bone Health, etc.), followed by Your Health Profile, Your Cellf Action Map™, and Your Action Plan™.

How to Read Your Health Profile

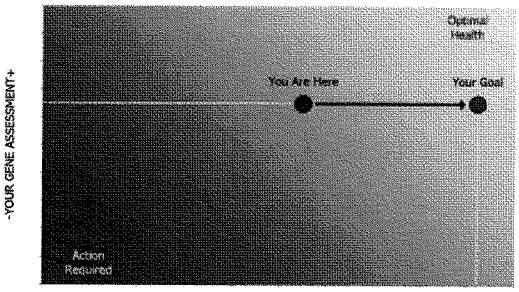
As part of your Cellf Assessment™, a total of 19 of your genes have been analyzed. These genes were then grouped into each of the five health areas reviewed in this booklet—Heart Health, Bone Health, Insulin Sensitivity, Antioxidant/Detoxification, and Inflammation—depending on which area the gene most affects. For example, your Bone Health Profile analyzes four genes associated with bone health. In each health section your results will be presented under the chart headings below.

Gene Analyzed	Role of the Gene	Genetic Variation Screened For	Variation Found in Your Gene	Percentage of Population with this Gene Variation*	Does Your Result Suggest an Impact on Bone Health?

How to Read Your Cellf Action Map

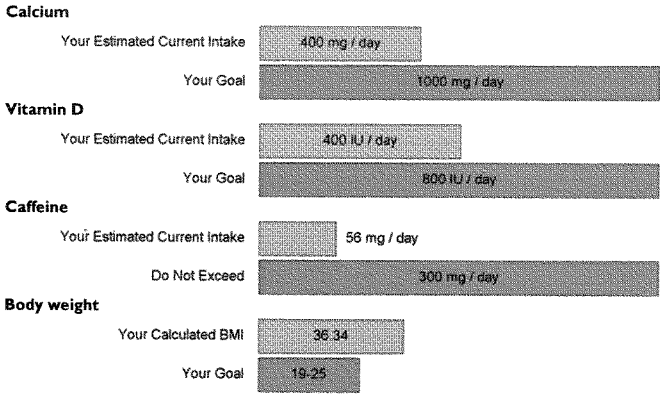
Your Gene Assessment and your Diet and Lifestyle Assessment were entered into the Genostic Rules Engine™ , an exclusive software program developed specifically for Cellf. This sophisticated analytical tool determines your position on your Cellf Action Map.

For each of the health categories, your current position on the Cellf Action Map— identified by the icon "You Are Here"—is plotted by the combination of your Gene Assessment (which cannot change) and your current Diet and Lifestyle Assessment (which can change depending on your current diet and lifestyle choices). Your optimal health goal is identified by the "Your Goal" icon. Importantly, your level of action required will be labeled **First Priority** (bottom section of map); **Second Priority** (middle section of map); and **Third Priority** (upper section of map). This prioritization will help you focus your efforts in the health areas which may have a greater impact on your health.
To measure your progress, please consult your healthcare professional.



How to Read Your Cellf Action Plan

Each section of your Cellf Assessment lays out an Action Plan comprised of specific diet, nutrition, and lifestyle recommendations that will help you reach your goal. Easy-to-read charts and graphs tell you what you need to modify (or not) to help you reach your health goals. The following is an example.

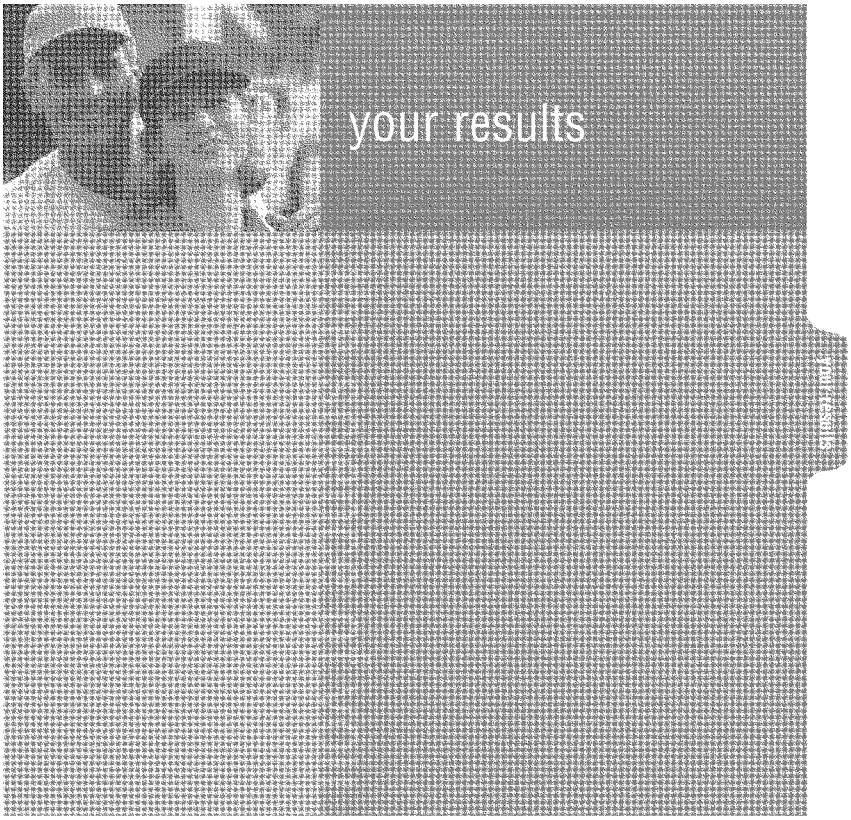


Important Information

The Cellf Assessment focuses only on the presence of genetic variations that have been shown in medical research to respond to dietary and environmental factors which can have an impact on overall health and well-being. The Cellf test does not analyze your genome (your complete genetic profile). The Cellf test is not a test for inherited disorders or diseases. The Cellf test does not screen for disorders caused by a defect in a single gene, such as Huntington's disease, cystic fibrosis or sickle cell anemia. The Cellf test does not test for inherited genes linked to a specific disease for example, genes associated with certain forms of breast cancer that run in families. The Cellf test will not tell you if you are ill. If you think you may be ill, you should consult your doctor. The Cellf test will not tell you if you will have reactions to certain medications or how medication prescribed by your physician will work, or if it will work.

The recommendations in your Cellf Assessment are based on combined information from your questionnaire and your personal genetic screening. Some nutrients when consumed in excess may be harmful rather than beneficial. If, based on your questionnaire answers, your intake greatly exceeds the commonly recommended levels, we will suggest that you reevaluate the amount of your intake of the nutrient(s) in excess.

If you have any questions regarding any aspect of our service, please contact us at 1-866-442-4380 from 8am to 4pm (Mountain Time), or by email at info@sciona.com. You can also find more information by visiting our website at www.sciona.com.


your results

Your Unique Cellf Results Begin Here

Let's get started. The following pages explain where you are right now regarding your genetics and current lifestyle. More importantly, they'll show you the steps that will lead you on the journey toward optimal health.

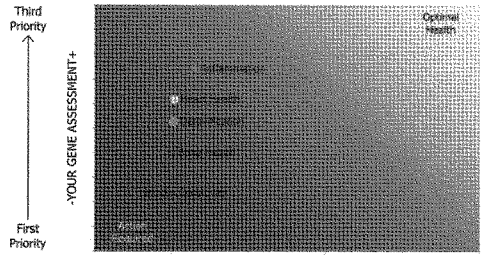
We've analyzed 19 of your genes in the five major health areas—bone health, heart health, insulin sensitivity, inflammation, and antioxidant/detoxification function—along with the lifestyle questionnaire you sent us. Using our Genostic Rules Engine™, we combined this information to give you an in-depth assessment of what you can do now to take an active role in your overall health.

The Overall Cellf Action Map™ overview on the right plots your current assessment and your optimal health potential for the five health areas. Each of these areas will be individually mapped out in the following sections. In addition, we've made recommendations, including changes you can make to your diet, nutritional supplements, exercise, and more, to reach your health goals. Each section is also detailed with maps, charts, and easy-to-understand information.

What should you do first? Look on page 14 for "Your Priorities" and learn how you can make the most immediate, positive impact on your health.

Take action now. Every step you take leads you one step closer to your goal!

Overall Cellf Action Map



Look for "Your Priorities" on the next page.

Your Priorities

First Priority

Your first area of focus should be Insulin Sensitivity. Based on your gene and lifestyle assessment, we recommend that you:

- Decrease your intake of high glycemic load (GL) carbohydrates
- Reduce your consumption of saturated fats
- Increase your intake of omega-3 fatty acids
- Reduce your weight; the ideal BMI is between 19 and 25
- Increase your levels of exercise

Second Priority

Your second area of focus should be Bone Health and Antioxidant/Detoxification function. Based on your gene and lifestyle assessment, we recommend that you:

- Increase your calcium intake
- Increase your vitamin D intake
- Decrease your caffeine consumption
- Increase your consumption of cruciferous vegetables such as broccoli or cauliflower
- Increase your consumption of allium vegetables such as garlic or onion
- Increase your consumption of foods high in antioxidants such as vitamins A, C, and E
- Stop smoking

Third Priority

Your third area of focus should be Heart Health and Inflammation. Based on your gene and lifestyle assessment, we recommend that you:

- Increase your consumption of foods rich in B vitamins including folate, vitamin B6, and vitamin B12
- Reduce your intake of cholesterol

* Please note that your questionnaire was not completely filled out, and this may have an impact on the accuracy of our estimations of your lifestyle and nutritional practices.

BONE HEALTH

Bone Health Overview

Your Personal Analysis

We have analyzed four of your genes that play an important role in determining how your body manages overall bone health. In analyzing your diet and lifestyle in relation to your genes, we assessed seven key action areas. The chart on the following page details your personal genetic profile, followed by specific recommendations just for you, based on your genes, diet, and lifestyle.

Remember, this advice is just for you and not applicable to others. The background information below will help you understand your personal bone health analysis.

A Brief Overview of Bone Health

Surprisingly, bones are not a fixed structure; in fact, your body breaks down and rebuilds bone all the time to make calcium available for vital functions. Your genes, diet, and lifestyle each are important factors to maintain balance in this process. An imbalance in one or more of these factors can lead to a breakdown in the creation of new bone tissue.

In our analysis, we may have identified certain variations in one or more of your bone health genes which can lead to the formation of altered proteins that can have an effect on your bone structure. These altered proteins may lead to bone loss, particularly if your diet lacks certain nutrients vital for bone health or if you are not physically active enough. Another contributing factor is age. From thirty on, both men and women naturally start losing bone mass. This is particularly marked in women after menopause. This bone loss can be slowed with proper attention to nutrition and lifestyle.

BONE HEALTH

Your Bone Health Profile

Your Bone Health Profile analyzes four genes that play an important role in determining how your body manages overall bone health.

Gene Analyzed	Role of the Gene in Bone Health	Genetic Variation Screened For	Variation Found in Your Gene	Percentage of Population with this Gene Variation*	Does Your Result Suggest an Impact on Bone Health?
VDR	Regulates Calcium and Vitamin D Roles in Bone Formation	TaqI	Yes	70.6	Yes
VDR		BsmI	No	69.6	Yes
VDR		FokI	N/A	63.8	N/A
COL1A1	Collagen Role in Bone Formation	GSp1T	No	21.0	No
IL-6	Old Bone Elimination New Bone Creation Cycle	G(-174)C	No	36.3	Yes
IL-6		G(-634)C	No	10.3	Yes
TNF-α		G(-308)A	No	16.5	No

*The population frequencies given are normalized for the U.S. population data from the U.S. 2002 Census Report. Population frequencies can vary for different ethnic groups, so for more detailed information, please turn to the Population Frequency Data Table in the Reference Section of your report.

N/A: Due to technical considerations we were not able to obtain a result for you at this location.

BONE HEALTH

Your Bone Health Results

Your Bone Health Gene Assessment and your current Diet and Lifestyle were entered into the Genostic Rules Engine™, an exclusive software program developed specifically for Cellf to determine your unique position on Your Action Map on the following page. Keep in mind that while you cannot change your genes, you can modify your diet, nutrition, and lifestyle to reach your optimal level of wellness.

Your Gene Assessment

Your Gene Assessment indicates that you have variations in specific genes in your Bone Health Profile that have been shown to impact calcium and vitamin D absorption. You have variations in specific genes in your Bone Health Profile associated with disruptions in the process of dissolving old bone and creating new bone.These results have been associated with negative impacts on bone health.

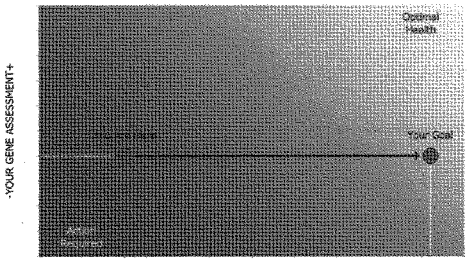
Your Diet and Lifestyle Assessment

We've identified specific diet and lifestyle factors important for bone health function; here's how you are doing with your own personal choices in these areas:

- Increase your calcium intake
- Increase your vitamin D intake
- Decrease your caffeine consumption
- Increase your intake of omega-3 fatty acids
- Reduce your weight; the ideal BMI is between 19 and 25
- Increase your levels of exercise

BONE HEALTH

Your Bone Health Cellf Action Map



How to Read Your Cellf Action Map

Your unique position on this Action Map indicates your Bone Health Profile is in the Second Priority range.

To measure your progress, please consult your healthcare professional.

BONE HEALTH

Your Cellf Action Plan

How to Read Your Cellf Action Plan

Your Cellf Assessment lays out an Action Plan comprised of specific diet, nutrition, and lifestyle recommendations that will help you reach your bone health goal. Easy-to-read charts and graphs tell you what you need to modify (or not) to take an active role in your overall health.

Your Results

We've analyzed your genes, diet and lifestyle and developed the following personalized plan that may help you achieve optimal bone health. Each of these actions is recommended to enable you to reach your goals. So start today!

Additional information for each Action Area is provided in the Reference section of your report.

1. Calcium

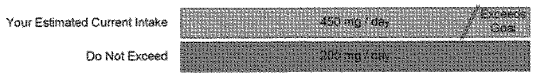
To help ensure adequate calcium absorption, we recommend that you increase your consumption of calcium-rich foods; aim for 1300 mg/day. To help you reach your goals, you may wish to choose a calcium supplement. If you are taking more than 500 mg a day, take calcium twice a day for maximum absorption.

2. Vitamin D

To help promote vitamin D absorption, we recommend that you increase your consumption of vitamin D-rich foods; your goal is 800 IU per day. Sunlight can also provide most of your vitamin D requirement. Ten to fifteen minutes of sun exposure at least two times per week to the face, arms, hands, or back without sunscreen can contribute to your goal of vitamin D levels.

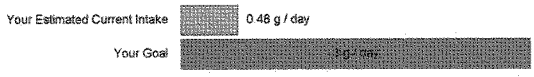
3. Caffeine

Your genetic profile has been associated with accelerated bone loss when excess caffeine is consumed. Based on your Diet and Lifestyle Assessment, we estimate your consumption of caffeine is above your maximum goal of 200 mg. We recommend that you decrease your current intake of caffeine and consider completely eliminating it from your diet.



4. Omega-3 fatty acids

Your genetic profile has been associated with a negative impact on bone regeneration, but the activity of some of these genes can be modulated by omega-3 fatty acids. Your intake of these essential fats is below your goal. Improve your omega-3 intake by eating fish (preferably oily) at least twice a week, including oils and foods rich in alpha-linolenic acid. In addition, you may benefit from taking a daily supplement containing at least 1 g of omega-3 fatty acids.



BONE HEALTH

5. Body weight

Your Gene Assessment indicates variations in genes that can impact bone health, and your body mass index is classed as overweight. Because this can have an impact on your health, we recommend you adopt lifestyle changes that will achieve a slow, sustainable, and healthy weight loss. You may wish to consult a registered dietician, nutritionist, or doctor to help you lose weight.

Your Calculated BMI	26.65
Your Goal	[illegible]

6. Physical activity

You should increase your levels of physical activity to help promote bone health. One reason to focus on exercise for bone health is that recent research has demonstrated a link between exercise and improved bone strength. We recommend moderate-intensity physical activity for 45-60 minutes five or more days a week.

Your Current Activity Level	Below goal
Your Goal	45 - 60 minutes at least 5 days a week

7. Tobacco

For optimal bone health, we recommend that you quit smoking and avoid tobacco smoke. Clinical studies have shown tobacco increases calcium excretion in the urine, and smokers have been shown to have decreased bone mass.

Note: If you suffer from any medical condition or are taking prescription drugs, consult with your doctor before taking any recommended supplement.

ANTIOXIDANT/DETOXIFICATION

Antioxidant/Detoxification Overview

Your Personal Analysis

We have analyzed six of your genes that play an important role in determining how your body manages overall antioxidant/detoxification functions. In analyzing your diet and lifestyle in relation to your genes, we assessed four key action areas. The chart on the following page details your personal genetic profile, followed by specific recommendations just for you, based on your genes, diet, and lifestyle.

Remember, this advice is just for you and not applicable to others. The background information below will help you understand your personal antioxidant/detoxification analysis.

A Brief Overview Of Antioxidant/Detoxification Activity

Antioxidant Activity

Antioxidant activity is an important component of the body's defense system. Oxygen is vital for life but can form highly reactive and potentially dangerous molecules, called free radicals. Free radicals can do great damage to our bodies; they attack DNA, proteins, and fats in our cells. Free radicals have been linked to a variety of common health disorders, including heart disease, chronic inflammation, and cancer, as well as accelerated aging. Our bodies have built-in defenses against free radicals: genes that make antioxidant enzymes that neutralize these highly reactive molecules.

In our analysis, we may have identified certain variations in your genes that produce and regulate antioxidant enzymes. As a result of these variations, these enzymes may have altered activity, which can have a negative impact on your health.

Detoxification Activity

Our bodies have built amazing defense systems to protect us from harmful substances, which can be found in the air we breathe and the food we eat. Detoxification genes are a very important part of these defense systems; these genes manufacture enzymes that process and remove the harmful substances or toxins. These toxins can come from food, water, air, or from the by-products of normal metabolism.

In our analysis, we may have identified certain variations in your detoxification genes that cause your detoxification enzymes to have altered activity. As a result, the removal of toxins from the body can be less efficient, leading to a build-up of toxins which can have a negative impact on your health.

Your Antioxidant/Detoxification Health Profile

Your Antioxidant/Detoxification Health Profile analyzes six genes that play an important role in determining how your body manages overall antioxidant/detoxification health.

Gene Analyzed	Role of the Gene in Antioxidant/ Detoxification Activity	Genetic Variation Screened For	Variation Found in Your Gene	Percentage Population with this Gene Variation*	Does Your Results Suggest an Impact on Antioxidant/ Detoxification Function?
eNOS	Vascular Function	G894T	Yes	35.6	Yes
GSTM1	Detoxification	(DEL)	Yes	69.0	Yes
GSTP1		A313G	Yes	34.8	Yes
		C341T	No	11.5	No
GSTT1		(DEL)	No	21.9	No
MnSOD	Destroys Free Radicals	C(-28)T	Yes	54.2	Yes
SOD3		C760G	No	<3	No

*The population frequencies given are normalized for the U.S. population data from the U.S. 2002 Census Report. Population frequencies can vary for different ethnic groups, so for more detailed information, please turn to the Population Frequency Data Table in the Reference Section of your report.

Note: (DEL) means that the gene is not present.

ANTIOXIDANT/DETOXIFICATION

Your Antioxidant/Detoxification Results

Your Antioxidant/Detoxification Gene Assessment and your current Diet and Lifestyle Assessment were entered into the Genostic Rules Engine™, an exclusive software program developed specifically for Cellf to determine your unique position on Your Cellf Action Map on the following page. Keep in mind that while you cannot change your genes, you can modify your diet, nutrition, and lifestyle to reach your optimal level of wellness.

Your Gene Assessment

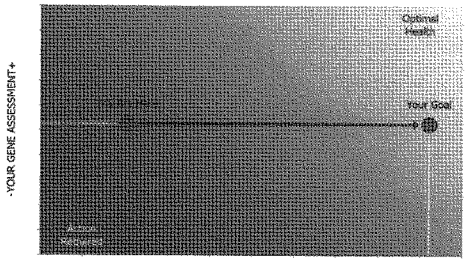
You have a variation that indicates altered capacity for production of nitric oxide, an important chemical that helps maintain vascular tone and blood flow. Your Gene Assessment indicates that you have variations that may lead to a reduced ability to clear toxins. You have variations in your genes important for antioxidant defenses which may lead to less efficient removal of free radical damage from your body.

Your Diet and Lifestyle Assessment

We've identified specific diet and lifestyle factors important for antioxidant/detoxification function; here's how you are doing with your own personal choices in these areas:

- Increase your consumption of cruciferous vegetables such as broccoli or cauliflower
- Increase your consumption of allium vegetables such as garlic or onion
- Increase your consumption of foods high in antioxidants such as vitamins A, C, and E
- Stop smoking

Your Antioxidant/Detoxification Cellf Action Map



How to Read Your Cellf Action Map

Your unique position on this Action Map indicates your Antioxidant/Detoxification Profile is in the Second Priority range.

To measure your progress, please consult your healthcare professional.

Your Cellf Action Plan

How to Read Your Cellf Action Plan

Your Cellf Assessment lays out an Action Plan comprised of specific diet, nutrition, and lifestyle recommendations that will help you manage your antioxidant/detoxification function. Easy-to-read graphs tell you what you need to modify (or not) to take an active role in your overall health.

Your Results

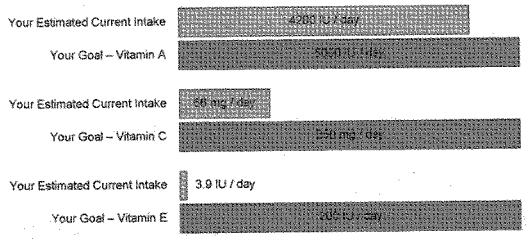
We've analyzed your genes, diet, and lifestyle and developed the following personalized plan that may help you achieve optimal antioxidant/detoxification function. Each of these actions is recommended to enable you to reach your goals. So start today!

Additional information for each Action Area is provided in the Reference section of your report.

ANTIOXIDANT/DETOXIFICATION

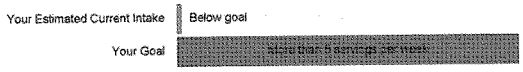
1. Antioxidant: vitamins A, C and E

Your genetic profile indicates a reduced ability to fight free radicals. Your Diet and Lifestyle Assessment indicates that you are not meeting your goals of antioxidant-rich foods in your daily diet. In order to improve your body's ability to fight free radicals, we recommend that you increase your intake of dietary antioxidants and consider choosing a high-quality, well-rounded nutritional supplement containing vitamins, minerals, and phytochemicals. Focus on the amounts as follows:



2. Cruciferous vegetables

Your genetic profile indicates a reduced ability to remove toxins. Cruciferous vegetables such as broccoli, cauliflower, and cabbage contain sulforophane, a very effective detoxification compound shown to have a dramatic effect on supporting the detoxification processes. Your Diet and Lifestyle Assessment indicates that you are not currently meeting your goal of these foods in your diet. Aim to increase your consumption as shown below. You can also look for a broccoli extract nutritional supplement that has been standardized to contain sulforophane.



ANTIOXIDANT/DETOXIFICATION

3. Allium vegetables

Based on your Diet and Lifestyle Assessment, you are not currently meeting your goal of levels of allium vegetables such as garlic and onion in your daily diet. The distinctive odor of these vegetables is created by the same chemicals that provide many of their beneficial properties, including aiding the body's antioxidant and detoxification systems. While all allium vegetables are beneficial to your health, most research has focused on garlic. Look for a garlic extract supplement which has been standardized for allicin content. For optimal support of your potentially reduced detoxification systems, aim to increase your consumption to the levels given below.

Your Estimated Current Intake	Below goal
Your Goal	[illegible]

4. Tobacco

We recommend you that quit smoking and avoid tobacco smoke. This is especially important, as your potential reduction of detoxification activity means that your body is less able to clear the toxic residues introduced by smoking. Smoking produces free radicals and your lowered inherent antioxidant activity means that you have less natural ability to remove these dangerous by-products of smoking. Finally, smoking can impact your vascular tone and function, and clinical studies have shown the genetic variation you have is more sensitive to tobacco smoke.

Note: If you suffer from any medical condition or are taking prescription drugs, consult with your doctor before taking any recommended supplement.

HEART HEALTH

Heart Health Overview

Your Personal Analysis

We have analyzed thirteen of your genes that play an important role in determining how your body manages overall heart health. In analyzing your diet and lifestyle in relation to your genes, we assessed nine key action areas. The chart on the following page details your personal genetic profile, followed by specific recommendations just for you, based on your genes, diet, and lifestyle. Remember, this advice is just for you and not applicable to others. The background information below will help you better understand your personal heart health analysis.

A Brief Overview of Heart Health

Heart health depends on a complex balance of environmental, dietary, and genetic factors. We have analyzed your DNA for a collection of genes that, according to the latest research, are believed to play an important part in heart health. These genes have a variety of functions.

Antioxidant Activity

Some provide antioxidant activity to help fight damage caused by free radicals. Free radicals are linked to the formation of plaque in the arteries. We may have identified variations in these genes, which clinical studies have shown can alter the production and regulation of the antioxidant enzymes, potentially affecting plaque formation.

Homocysteine Levels

You also have several genes that influence the levels of homocysteine in the blood. The latest research has shown that raised homocysteine may have a negative impact on heart health. Medical research has demonstrated that homocysteine levels may be kept at safe limits by ensuring optimum intake of B vitamins.

HEART HEALTH

Cholesterol Levels

In addition, you have a collection of genes that influence LDL and HDL cholesterol levels. Higher levels of LDL, or "bad" cholesterol, are associated with a negative impact on heart health.

Blood Flow

You also have genes that are important in the function of your blood vessels and your blood flow. We may have identified some variations in these genes that can lead to increased risk of high blood pressure due to constriction or tightening of the blood vessels.

Inflammation

Lastly, you have genes that are associated with the function of inflammatory response. While the inflammatory process is important for healing, variations in these genes can lead to reactions that are too strong or inappropriate in their timing, and can have a negative impact on heart health.

Your Heart Health Profile

Your Heart Health Profile analyzes thirteen genes that play an important role in determining how your body manages overall heart health.

Gene Analyzed	Role of the Gene in Heart Health	Genetic Variation Screened For	Variation Found in Your Gene	Percentage of Population with this Gene Variation*	Does Your Result Suggest an Impact on Heart Health?
MTHFR	Use of Folic Acid for DNA Synthesis or DNA Repair	C677T	No	28.7	No
		A1298C	No	30.0	No
MS_MTRR	Metabolism of Vitamin B_{12}	A66G	Yes	47.3	Yes
MTR	Removal of Homocysteine	A2756G	No	17.4	Yes
CBS	Metabolism of Vitamin B_6 and Removal of Homocysteine	C699T	No	28.0	Yes
MnSOD	Antioxidant Defense	C(-28)T	Yes	54.2	Yes
SOD3		C760G	No	<3	No
IL-6	Inflammatory Response	G(-174)C	No	36.3	No
TNF-α		G(-308)A	No	16.5	No
APOC3	Triglyceride Metabolism	C3175G	No	12.6	No
CETP	Cholesterol Metabolism	G279A	Yes	37.0	Yes
LPL		C1595G	No	9.9	Yes
eNOS	Blood Flow	G894T	Yes	35.6	Yes
ACE		I/DD	Yes	61.0	Yes

*The population frequencies given are normalized for the U.S. population data from the U.S. 2002 Census Report. Population frequencies can vary for different ethnic groups, so for more detailed information, please turn to the Population Frequency Data Table in the Reference Section of your report.

Note: (DEL) means that the gene is not present.

HEART HEALTH

Your Heart Health Results

Your Heart Health Gene Assessment and your current Diet and Lifestyle Assessment were entered into the Genostic Rules Engine™, an exclusive software program developed specifically for Cellf to determine your unique position on Your Cellf Action Map on the following page. Keep in mind that while you cannot change your genes, you can modify your diet, nutrition, and lifestyle to reach your optimal level of wellness.

Your Gene Assessment

Your Gene Assessment indicates that you have variations in genes that are important in the metabolism of B vitamins, including folate, vitamin B6, and vitamin B12. These variations make it important to keep your levels of B vitamins up to maintain optimum homocysteine levels and help promote heart health. You have a variation in your antioxidant defense genes. Maintaining optimum levels of foods rich in antioxidants can help you combat the damaging effects of free radicals on your cardiovascular system, especially plaque build-up in your blood vessels. You do not have variations in the specific inflammation genes included in your screen. You have variations in your cholesterol and triglyceride metabolizing genes. To help avoid high cholesterol and triglyceride levels, you will need to pay particular attention to the levels of unsaturated and saturated fats in your diet. You have variations in your genes that impact blood flow. This can affect constriction or tightening of your blood vessels, which in turn can have an impact on blood pressure. However, this can be modulated by maintaining adequate levels of omega-3 fatty acids in your diet.

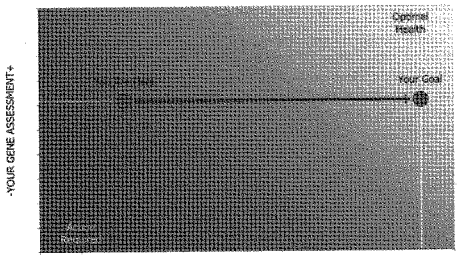
Your Diet and Lifestyle Assessment

We've identified specific diet and lifestyle factors important for heart health function; here's how you are doing with your own personal choices in these areas:

- Increase your consumption of foods rich in B vitamins including folate, vitamin B6, and vitamin B12
- Increase your consumption of foods high in antioxidants such as vitamins A, C, and E
- Reduce your consumption of saturated fats
- Increase your intake of omega-3 fatty acids
- Reduce your intake of cholesterol
- Reduce your weight; the ideal BMI is between 19 and 25
- Increase your levels of exercise

HEART HEALTH

Your Heart Health Celif Action Map



How to Read Your Celif Action Map

Your unique position on your Action Map indicates that your Heart Health Profile is in the Third Priority range.

To measure your progress, please consult your healthcare professional.

HEART HEALTH

Your Cellf Action Plan

How to Read Your Cellf Action Plan

Your Cellf Assessment lays out an Action Plan comprised of specific diet, nutrition, and lifestyle recommendations that will help you reach your heart health goals. Easy-to-read graphs tell you what you need to modify (or not) to take control of your heart health.

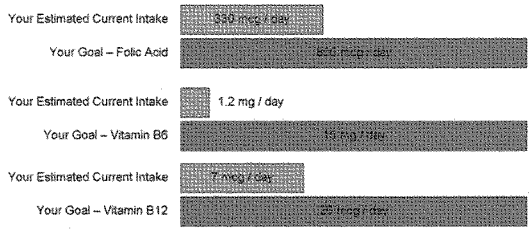
Your Results

We've analyzed your genes, diet, and lifestyle and developed the following personalized plan that may help you achieve optimal heart health. Each of these actions is recommended to enable you to reach your goals. So start today!

Additional information for each Action Area is provided in the Reference section of your report.

1. B vitamins: folic acid, vitamin B_6, and vitamin B_{12}

Your Genetic Profile indicates you have variations in the B vitamin metabolizing genes included in your Heart Health screen. This makes it very important for you to meet your goals of levels of these vitamins to keep your homocysteine levels low and help promote heart health. Your Diet and Lifestyle Assessment indicates that you are not meeting one or more of your goals of B vitamins in your diet, as shown below. You may wish to use supplements to ensure you meet your goals of B vitamins. We recommend you choose a high quality supplement with USP certification.



HEART HEALTH

2. Antioxidant: Vitamins A, C, and E

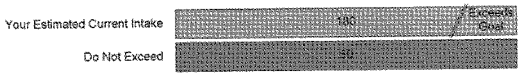
Your genetic profile indicates a reduced ability to fight free radicals. Free radicals may cause damage to your cardiovascular system. Your Diet and Lifestyle Assessment indicates that you are not currently meeting all of your goals of levels of antioxidant-rich foods in your diet. In order to improve your ability to fight free radicals, we recommend that you meet your goals of antioxidant-rich foods. You may also wish to choose a high-quality, well-rounded nutritional supplement containing vitamins, minerals, and phytochemicals. Focus on amounts as follows:

Your Estimated Current Intake	4,200 IU / day
Your Goal – Vitamin A	[illegible]
Your Estimated Current Intake	86 mg / day
Your Goal – Vitamin C	[illegible]
Your Estimated Current Intake	3.9 IU / day
Your Goal – Vitamin E	[illegible]

HEART HEALTH

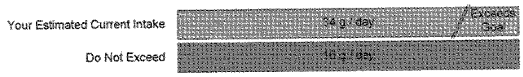
3. Glycemic load-carbohydrates

According to our estimates, you are not within your goal of glycemic carbohydrates in your diet. We recommend that you choose low glycemic load (GL) carbohydrates including whole grains and foods high in fiber to promote heart health. Research has shown generous portions of whole grains help promote heart health. High glycemic load carbohydrates do not offer the same benefit because processing removes the bran from the grain and loses the health benefit. Aim to include at least three to five portions of low glycemic load whole grains daily.



4. Saturated fats

Your Genetic Profile shows variations in genes involved in cholesterol and triglyceride metabolism. According to your Diet and Lifestyle Assessment, you are currently exceeding your goal on levels of saturated fats in your diet. A high intake of saturated fats can have a negative impact on heart health. Maintain your saturated fat intake to less than 7% of your total calories and keep total fat—unsaturated and saturated—to less than 30% of your calories.



5. Cholesterol

Your genetic profile indicates variations in genes involved in cholesterol and lipid metabolism. Your Diet and Lifestyle Assessment indicates that you are currently exceeding your goal of levels of cholesterol in your diet. We recommend you reduce your cholesterol intake to less than 200 mg/day, so that you do not overwhelm your body's altered ability to metabolize this substance. Consider plant sterols and fiber supplements, which have been shown to reduce cholesterol levels.

6. Omega-3 fatty acids

Omega-3 fatty acids are beneficial for variations in genes important for blood flow. According to our estimates, you are not currently reaching your goal of omega-3 fatty acids in your diet. Improve your omega-3 intake by eating fish (preferably oily) at least twice a week, including oils and foods rich in alpha-linolenic acid. You may wish to choose at least 1 g of an omega-3 supplement to help meet your goal.

7. Body weight

Your body mass index is classed as overweight. Body mass plays an important role in heart health, so it's important to monitor and maintain a BMI between 19 and 25.

Your Calculated BMI	29.55
Your Goal	19 - 25

8. Tobacco

For optimum heart health, we recommend that you quit smoking and avoid passive smoke. You have variations in your antioxidant defense genes, which may reduce your ability to remove the free radicals produced by cigarette smoke. You also have variations in genes involved in blood flow regulation, which can lead to increased blood pressure in the presence of cigarette smoke.

9. Physical activity

Your current level of exercise is below your goal. For optimum heart health, it is important that you participate in regular physical activity—especially as your Genetic Profile indicates that you have variations in genes important for blood flow that respond particularly well to exercise. Clinical studies have shown that individuals with these variations tend to have lowered blood pressure and cholesterol levels when actively exercising. We recommend moderate-intensity physical activity for 45-60 minutes on five or more days of the week.

Your Current Activity Level	Below goal
Your Goal	45 - 60 minutes at least 5 days a week

Note: If you suffer from any medical condition or are taking prescription drugs, consult with your doctor before taking any recommended supplement.

INFLAMMATION

Inflammation Health Overview

Your Personal Analysis

We have analyzed six of your genes that play an important role in determining how your body manages inflammation. In analyzing your diet and lifestyle in relation to your genes, we assessed four key action areas. The chart on the following page details your personal genetic profile, followed by specific recommendations just for you, based on your genes, diet, and lifestyle. Remember, this advice is just for you and not applicable to others. The background information below will help you understand your personal inflammation analysis.

A Brief Overview of Inflammation

Inflammation is an essential, protective response of your body's tissues to disease, injury, infection, or the presence of a protein to which you have an allergic reaction. For example, the redness and swelling around a wound or an infected area are signals that your body's normal healing processes are functioning to repair the damage.

The release of these natural healing substances is controlled by genes that govern inflammation. Normally, when the need for healing is completed, these genes "turn off" until they are needed again and the inflammation subsides. However, sometimes these genes remain "on" longer than they should, and as a result, trigger reactions that are too strong or unnecessary.

Your Inflammation Profile

Your Inflammation Profile analyzes six genes that play an important role in determining how your body manages overall inflammation. This chart details our findings.

Gene Analyzed	Role of the Gene in Inflammation	Genetic Variation Screened For	Variation Found in Your Gene	Percentage of Population with this Gene Variation*	Does Your Result Suggest an Impact on Inflammation?
GSTM1	Detoxification	(DEL)	Yes	69.0	Yes
GSTP1		A313G	Yes	34.8	Yes
GSTT1		(DEL)	No	21.9	No
MnSOD	Destroys Free Radicals	C(-28)T	Yes	54.2	Yes
IL-6	Inflammatory Response	G(-174)C	No	36.3	No
IL-6		G(-634)C	No	10.3	No
TNF-α		G(-308)A	No	16.5	No

*The population frequencies given are normalized for the U.S. population data from the U.S. 2002 Census Report. Population frequencies can vary for different ethnic groups, so for more detailed information, please turn to the Population Frequency Data Table in the Reference Section of your report.

Note: (DEL) means that the gene is not present.

INFLAMMATION

Your Inflammation Results

Your Inflammation Gene Assessment and your current Diet and Lifestyle Assessment were entered into the Genostic Rules Engine™, an exclusive software program developed specifically for Cellf to determine your unique position on Your Action Map on the following page. Keep in mind that while you cannot change your genes, you can modify your diet, nutrition, and lifestyle to reach your optimal level of wellness.

Your Gene Assessment

Your Gene Assessment indicates that you have variations in the specific genes important in your inflammatory response; this can result in an increased inflammatory state. You do not have variations in the specific genes in your Inflammation Profile that have been shown to produce an increased expression of inflammation. You have variations that can lead to reduced ability to clear toxins. One of your natural antioxidant genes has a variation, making it less able to remove the free radicals that can contribute to an inflammatory reaction.

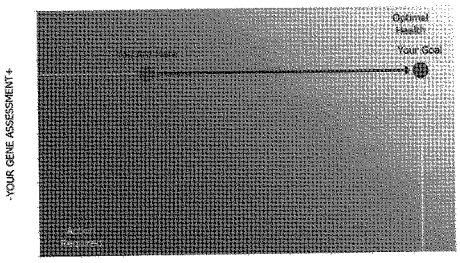
Your Diet and Lifestyle Assessment

We've identified specific diet and lifestyle factors important for inflammation function; here's how you are doing with your own personal choices in these areas:

- Increase your consumption of foods high in antioxidants such as vitamins A, C, and E
- Increase your intake of omega-3 fatty acids
- Reduce your weight; the ideal BMI is between 19 and 25

INFLAMMATION

Your Inflammation Cellf Action Map



How to Read Your Cellf Action Map

Your unique position on this Action Map indicates your Inflammation Profile is in the Third Priority range.

To measure your progress, please consult your healthcare professional.

Your Cellf Action Plan

How to Read Your Cellf Action Plan

Your Cellf Assessment lays out an Action Plan comprised of specific diet, nutrition, and lifestyle recommendations that will help you manage your inflammation process. Easy-to-read graphs tell you what you need to modify (or not) to help maintain a healthy inflammation response.

Your Results

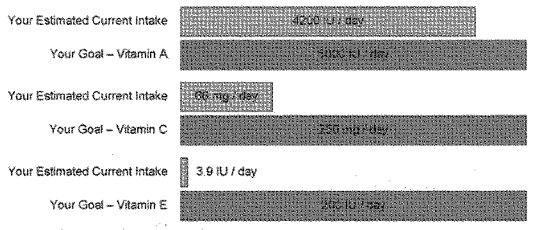
We've analyzed your genes, diet, and lifestyle and developed the following personalized plan that may help you manage your inflammation process. Each of these actions is recommended to enable you to reach your goals. So start today!

Additional information for each Action Area is provided in the Reference section of your report.

INFLAMMATION

1. Antioxidant: Vitamins A, C, and E

Your genetic profile indicates a reduced ability to fight free radicals and your Diet and Lifestyle Assessment indicates that you are not currently meeting all of your antioxidant-rich food goals. To improve your body's ability to fight free radicals, we recommend that you increase your intake of antioxidant-rich foods and choose a high-quality, well-rounded nutritional supplement containing vitamins, minerals, and phytochemcials. Focus on the amounts as follows:



INFLAMMATION

2. Omega-3 fatty acids

Omega-3 fatty acids are essential components of a healthy diet and can have an impact on your inflammatory function. According to our estimates, you are not currently reaching your goals of levels of these essential fatty acids in your diet. Improve your omega-3 intake by eating fish (preferably oily) at least twice a week, and include oils and foods rich in alpha-linolenic acid. If you are unable to obtain enough of these essential fats through diet alone, you may wish to add an omega-3 or fish oil supplement.

Your Estimated Current Intake	0.48 g / day
Your Goal	5 g / day

3. Body weight

It is important to monitor your BMI, and to achieve and maintain a BMI between 19 and 25. Obesity has been linked with a long-term, low-grade inflammatory state that can alter body fat. People who are significantly overweight have been shown to have increased levels of cytokines, a marker for increased inflammation, in their blood. You have gene variants that can lead to increased levels of these cytokines, so attaining an optimal weight is important for your health.

Your Calculated BMI	26.65
Your Goal	19 - 25

INFLAMMATION

4. Tobacco

For optimal inflammatory function, we recommend that you quit smoking and avoid passive tobacco smoke. Clinical studies have shown tobacco increases free radical production and the production of toxic by-products that can lead to an increased inflammatory state. Your potential reduction of detoxification activity means that your body is less able to clear the residues from smoking. Smoking produces free radicals and your lowered inherent antioxidant activity means that you have less natural ability to remove these dangerous by-products of smoking.

Note: If you suffer from any medical condition or are taking prescription drugs, consult with your doctor before taking any recommended supplement.

Insulin Sensitivity Overview

Your Personal Analysis

We have analyzed five of your genes that play an important role in determining how your body manages overall insulin sensitivity. In analyzing your diet and lifestyle in relation to your genes, we assessed five key action areas. The chart on the following page details your personal genetic profile, followed by specific recommendations just for you, based on your genes, diet, and lifestyle.

Remember, this advice is just for you and not applicable to others. The background information below will help you understand your personal insulin sensitivity analysis.

A Brief Overview of Insulin Sensitivity

Normally, food is absorbed into the bloodstream in the form of sugars such as glucose, fats, and other basic substances. An increase in glucose in the bloodstream signals the pancreas to release the hormone insulin. Insulin attaches itself to cells where it facilitates the transfer of glucose from the bloodstream into the cells for storage as glycogen and later for use as energy, or fuel, by the body's cells.

Insulin sensitivity refers to the ability of the body's cells to respond to the action of the insulin hormone. In the case of reduced sensitivity, the pancreas secretes more insulin, resulting in high levels of insulin in the bloodstream. Physicians believe that the loss of sensitivity to insulin may play an important role in some of the most common health disorders including type 2 diabetes, high blood pressure, heart disease, and disrupted fat metabolism.

In our analysis, we have looked at several different genes linked to insulin sensitivity, each of which play diverse roles in the body, and some of which at first sight do not appear to be directly related to insulin. For example, the vitamin D receptor gene (VDR), as well as being important in bone health, also plays a role in insulin secretion and the maintenance of glucose tolerance.

Your Insulin Sensitivity Health Profile

Your Insulin Sensitivity Health Profile analyzes five genes that play an important role in determining how your body manages overall sensitivity to insulin.

Gene Analyzed	Role of the Gene in Insulin Sensitivity	Genetic Variation Screened For	Variation Found in Your Gene	Percentage of Population with this Gene Variation	Does Your Result Suggest an Impact on Insulin Sensitivity?
VDR	Mechanism of Insulin Secretion	TaqI	Yes	70.6	Yes
VDR		BsmI	No	69.6	Yes
IL-6	Inflammatory Response; Response of Cells to Insulin	G(-174)C	No	36.3	Yes
TNF-α		G(-308)A	No	16.5	No
PPARγ2	Glucose and Lipid Metabolism	Pro12Ala	No	10.3	Yes
ACE	Blood Pressure Regulation	II/DD	Yes	61.0	Yes

**The population frequencies given are normalized for the U.S. population data from the U.S. 2002 Census Report. Population frequencies can vary for different ethnic groups, so for more detailed information, please turn to the Population Frequency Data Table in the Reference Section of your report.*

Your Insulin Sensitivity Results

Your Insulin Sensitivity Gene Assessment and your current Diet and Lifestyle Assessment were entered into the Genostic Rules Engine™, an exclusive software program developed specifically for Cellf to determine your unique position on Your Cellf Action Map on the following page. Keep in mind that while you cannot change your genes, you can modify your diet, nutrition, and lifestyle to reach your optimal level of wellness.

Your Gene Assessment

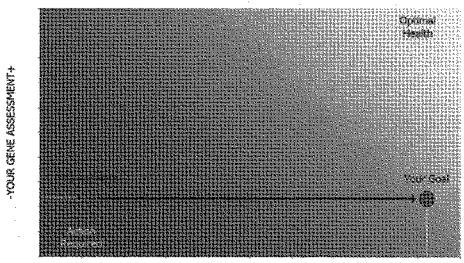
Your Gene Assessment indicates that you have genetic variations that can have an impact on elevated insulin and glucose release into your bloodstream. Your Insulin Sensitivity Profile indicates you have variations in your genes that increase insulin resistance in your body's fat cells. These results suggest that you should focus on diet and lifestyle choices that promote healthy sensitivity to insulin.

Your Diet and Lifestyle Assessment

We've identified specific diet and lifestyle factors important for insulin senstivity function; here's how you are doing with your own personal choices in these areas:

- Decrease your intake of high glycemic load (GL) carbohydrates
- Reduce your consumption of saturated fats
- Increase your intake of omega-3 fatty acids
- Reduce your weight; the ideal BMI is between 19 and 25
- Increase your levels of exercise

Your Insulin Cellf Action Map



How to Read Your Cellf Action Map

Your unique position on this Action Map indicates your Insulin Sensitivity Profile is in the First Priority range.

To measure your progress, please consult your healthcare professional.

INSULIN SENSITIVITY

Your Cellf Action Plan

How to Read Your Cellf Action Plan

Your Cellf Assessment lays out an Action Plan comprised of specific diet, nutrition, and lifestyle recommendations that will help you manage your insulin sensitivity. Easy-to-read graphs tell you what you need to modify (or not) to help manage your health and well-being.

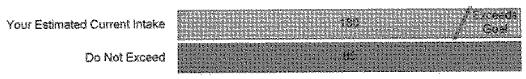
Your Results

We've analyzed your genes, diet, and lifestyle and developed the following personalized plan that may help you manage your risk for developing insulin sensitivity. Each of these actions is recommended to enable you to reach your goals. So start today!

Additional information for each Action Area is provided in the Reference section of your report.

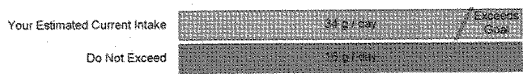
1. Glycemic load-carbohydrates

We recommend you significantly decrease the glycemic load (GL) in your diet, choose low glycemic load whole grains and foods high in fiber. This may help promote healthy insulin health, based on the variations in your genetic Insulin Sensitivity Profile. Whole grains and high-fiber foods are digested slowly, while most refined foods and simple carbohydrates, such as sugar, usually cause glucose levels to rise quickly.



2. Saturated fats

According to your Diet and Lifestyle Assessment, you are exceeding your goal of saturated fats in your diet. High levels of saturated fats can have a negative impact on insulin sensitivity. Reduce your saturated fat intake to less than 7% of your total calories and keep total fat—unsaturated and saturated—to less than 30% of your calories. Different fatty acids have been shown to alter the way some of the variations in your insulin sensitivity genes express themselves.



3. Omega-3 fatty acids

Your genetic profile includes variations that can have an impact on response to insulin, but studies have shown that the expression of the gene variations can be modulated by omega-3 fatty acids. According to our estimates, you are not currently reaching your goal of omega-3 fatty acids in your diet. Improve your omega-3 intake by eating fish (preferably oily) at least twice a week, including oils and foods rich in alpha-linolenic acid. You may wish to choose a supplement that contains at least 1g of omega-3 fatty acids.

Your Estimated Current Intake	0.48 g / day
Your Goal	1 g / day

4. Body weight

Your ideal body mass index is within the range of 19–25. We recommend that you adopt lifestyle changes that will help you achieve a slow, sustainable, and healthy weight loss. High body weight is strongly associated with reduced insulin sensitivity, but which can be restored by weight loss. You may wish to consult a registered dietician, nutritionist, or doctor who can help you to lose weight.

Your Calculated BMI	26.55
Your Goal	19–25

5. Physical activity

Your Diet and Lifestyle Assessment shows that your exercise levels are below your goal and should be increased. Experts recommend regular physical activity for wide-ranging health benefits. Recent research has shown that exercise helps maintain insulin sensitivity. We recommend moderate-intensity physical activity for 45-60 minutes five or more days of the week to help promote optimum insulin sensitivity.

Your Current Activity Level	Below goal
Your Goal	[illegible]

Note: If you suffer from any medical condition or are taking prescription drugs, consult with your doctor before taking any recommended supplement.

SUMMARY TABLE

Your Personal Results Summarized for Your Healthcare Practitioner

Below is a summary of your personalized results written for your healthcare practitioner, should you wish to share your information with this individual. We encourage you to share your results with your healthcare practitioner as we have found that such professionals can play a very important role in helping you work toward achieving your personal optimal health goals.

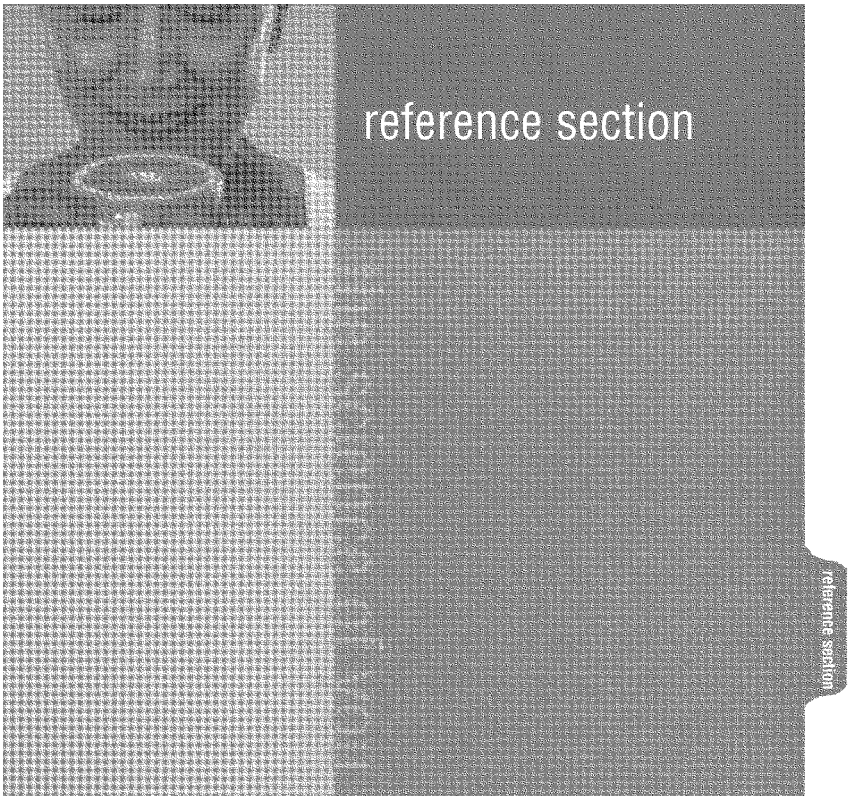
Gene Name	Genetic Variation Screened For	Your Genetic Results	Impact on Health Area	Area of Activity
MTHFR	C677T	CC	No	Heart Health
MTHFR	A1298C	AA	No	Heart Health
MS-MTRR	A66G	A/G	Yes	Heart Health
MTR	A2756G	AA	Yes	Heart Health
CBS	C699T	CC	Yes	Heart Health
MnSOD	C(-28)T	C/T	Yes	Heart Health
			Yes	Antioxidant/Detoxification
			Yes	Inflammation
SOD3	C760G	CC	No	Heart Health
			No	Antioxidant/Detoxification
GSTM1	Present or Deleted	Deleted	Yes	Antioxidant/Detoxification
			Yes	Inflammation
GSTT1	Present or Deleted	Present	No	Antioxidant/Detoxification
			No	Inflammation
GSTP1	A313G	A/G	Yes	Antioxidant/Detoxification
			Yes	Inflammation
GSTP1	C341T	CC	No	Antioxidant/Detoxification
IL-6	G(-174)C	GG	Yes	Bone Health
			Yes	Insulin Sensitivity
			No	Heart Health
			No	Inflammation

Gene Name	Genetic Variation Screened For	Your Genetic Results	Impact on Health Area	Area of Activity
IL-6	G(-634)C	GG	Yes	Bone Health
			No	Inflammation
APOC3	C3175G	CC	No	Heart Health
CETP	G279A	G/A	Yes	Heart Health
LPL	C1595G	CC	Yes	Heart Health
eNOS	G894T	TT	Yes	Heart Health
			Yes	Antioxidant/Detoxification
ACE	Insertion/Deletion	Deletion	Yes	Heart Health
			Yes	Insulin Sensitivity
VDR	Bsm1	AA	Yes	Bone Health
			Yes	Insulin Sensitivity
VDR	Taq1	CC	Yes	Bone Health
			Yes	Insulin Sensitivity
VDR	Fok1	N/A	N/A	Bone Health
COL1A1	G5p1T	GG	No	Bone Health
TNF-α	G(-308)A	GG	No	Bone Health
			No	Heart Health
			No	Insulin Sensitivity
			No	Inflammation
PPAR-γ2	Pro12 Ala	CC	Yes	Insulin Sensitivity

N/A: Due to technical considerations we were not able to obtain a result for you at this location.

SUMMARY TABLE

Dietary/Lifestyle Factors	Jamie's Action Plan	
	Your Estimated Diet and Lifestyle Results	Your Nutrition and Lifestyle Goals
Folate (mcg)	330 mcg / day	800 mcg / day
Vitamin B_6 (mg)	1.2 mg / day	15 mg / day
Vitamin B_{12} (mcg)	7 mcg / day	20 mcg / day
Cruciferous Vegetables	Below goal	More than 5 servings per week
Allium Vegetables	Below goal	Daily serving
Vitamin A (IU)	4200 IU / day	5000 IU / day
Vitamin C (mg)	66 mg / day	250 mg / day
Vitamin E (IU)	3.9 IU / day	200 IU / day
Calcium (mg)	570 mg / day	1300 mg / day
Vitamin D (IU)	480 IU / day	800 IU / day
Caffeine (mg)	450 mg / day	< 200 mg / day
Carbohydrates: Glycemic Load (GL)	180	< 80
Saturated Fat (g)	34 g / day	< 16 g / day
Cholesterol (mg)	490 mg / day	< 200 mg / day
Omega-3 Fatty Acids (g)	0.48 g / day	3 g / day
Tobacco	Yes	Quit smoking to complement your personal profile
BMI	26.55	19 - 25
Physical Activity	Below goal	45 - 60 minutes at least 5 days a week


reference section
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ACTION AREAS

As part of your Cellf Action Plan, we advise you to eat foods that contain certain nutrients. Below is a quick reference guide that will help you choose the right foods to achieve your goals.

ANTIOXIDANTS: Vitamins A, C, and E

WHY ARE VITAMINS A, C, AND E IMPORTANT FOR YOUR HEALTH?

Vitamins are organic molecules essential for normal metabolism, growth and development, and for the regulation of cell function. Because they generally cannot be synthesized by human cells, vitamins must be supplied through your diet or in a supplement. As part of your Cellf Action Plan, we advise you eat foods rich in these vitamins to help improve your antioxidant/detoxification function.

VITAMIN A (RETINOL) AND BETA CAROTENE

Vitamin A helps in the formation and maintenance of healthy teeth, skeletal and soft tissue, mucous membranes, and skin. It also generates pigments in the retina and promotes good vision, especially in dim light. Beta carotene, a precursor of vitamin A, is a potent antioxidant. Vitamin A is a fat soluble vitamin and can be stored in the body for a long time, so it is very important to limit intake to safe levels, generally considered to be below 10,000 IU per day.

FOOD EXAMPLES

Vitamin A is found in animal sources such as eggs, milk, cheese, cream, meat, liver, kidney, cod, and halibut fish oil. Its precursor, beta carotene, is found in plant foods such as carrots, pumpkin, sweet potatoes, winter squashes, cantaloupe, pink grapefruit, apricots, broccoli, spinach, and most dark green, leafy vegetables. The more intense the color of a fruit or vegetable, the higher its beta carotene content. The body regulates the conversion of beta carotene to vitamin A based upon its needs.

ANTIOXIDANTS: Vitamins A, C, and E (continued)

VITAMIN C (ASCORBIC ACID)

Vitamin C is vital for the formation of teeth, bone, cartilage, and maintaining healthy gums. It also plays a significant role in supporting your immune system.

FOOD EXAMPLES

Rich sources of vitamin C are citrus fruits, kiwi, guavas, strawberries, tomatoes, green peppers, and alfalfa sprouts.

VITAMIN E (ALPHA-TOCOPHEROL)

Vitamin E protects unsaturated fats in cells from damage. It is also important in the formation of red blood cells and the use of vitamin K, which is essential for blood clotting.

FOOD EXAMPLES

Vitamin E can be found in wheat germ, corn, nuts, seeds, olives, spinach, asparagus, and other green, leafy vegetables, vegetable oils (corn, sunflower, soybean, and cottonseed), and products made from vegetable oils such as margarine.

VITAMIN D

WHY IS VITAMIN D IMPORTANT FOR YOUR HEALTH?

Vitamin D maintains normal blood levels of calcium and phosphorus and aids in calcium absorption, helping to form strong bones. Although this vitamin is found in certain foods, it can also be created in the skin after exposure to ultraviolet (UV) rays from the sun. Without vitamin D, bones can become thin, brittle, soft, or misshapen. Long-term deficiency increases the risk of osteoporosis-related fractures and can lead to a skeletal condition characterized by weakened bones, known as rickets in children and as osteomalacia in adults. The latest medical research suggests that by treating deficiency with diet changes or a vitamin D supplement, people can reduce bone loss.

TIPS AND ADVICE

- Dietitians and nutritionists recommend adults consume at least ten micrograms (400 IU) of vitamin D daily.
- Milk is the richest source of vitamin D. In the U.S., milk is fortified with 10 micrograms (400 IU) of vitamin D per quart.
- Although milk is fortified with vitamin D, dairy products made from milk such as cheese, yogurt, and ice cream are generally not fortified with this vitamin. Vitamin D is present in these foods in smaller amounts than in milk.
- Apart from milk, various foods such as breakfast cereals, pastries, breads, crackers, and cereal grain bars may be fortified with vitamin D. If you eat these foods, check the labels for their vitamin D content.
- The body manufactures vitamin D when exposed to sunshine; ten to fifteen minutes of sunshine at least two times a week is adequate to ensure sufficient production of vitamin D.

FOOD EXAMPLES

Fortified foods are the major dietary sources of vitamin D. The richest natural source is milk, followed by fish oils and fatty fish such as sardines, tuna, salmon, mackerel, and herring.

B VITAMINS AND FOLIC ACID

WHY ARE B VITAMINS AND FOLIC ACID IMPORTANT FOR YOUR HEALTH?

Vitamins are organic molecules essential for normal metabolism, growth and development, and for the regulation of cell function. Since they generally cannot be synthesized by human cells, vitamins must be supplied in the diet or in a supplement. Certain B vitamins are particularly important and work together with folic acid to support heart health.

VITAMIN B_6 (PYRIDOXINE)

Vitamin B_6 plays a role in the synthesis and transformation of amino acids, in the multiplication of cells, and in the production of red blood cells, immune cells, and neurotransmitters. It is also required for the chemical reactions involving proteins. The higher the protein intake, the greater the need for vitamin B_6. It is a partner of folate and B_{12} in numerous processes.

FOOD EXAMPLES

Vitamin B_6 is obtained from poultry, pork, eggs, liver, kidney, beans, legumes, whole grains, spinach, carrots, peas, walnuts, sunflower seeds, and wheat germ.

VITAMIN B_{12} (CYANOCOBALAMIN, DIBENCOZIDE AND METHYLCOBALAMIN)

Vitamin B_{12}, like the other B vitamins, is important for cell growth and for the formation of red blood cells, as well as for the maintenance of the central nervous system.

FOOD EXAMPLES

Vitamin B_{12} can be found in liver, kidney, red meat, poultry, fish, eggs, and dairy products. Vegan sources include yeast extracts and soy milk.

FOLATE ("FOLIC ACID" IN SYNTHETIC FORM)

Folate, together with vitamins B_6 and B_{12}, enables the synthesis of new proteins. It is necessary for normal cell function and tissue growth, for the production of red blood cells and for the synthesis, function, and protection of DNA. It is involved in the normal performance of many neurotransmitters that regulate mood and behavior. Folate is also a critical vitamin in the proper metabolism of homocysteine.

FOOD EXAMPLES

Folate occurs in large amounts in liver and in lower concentrations in beef, lamb, pork, dark green, leafy vegetables (such as spinach, turnip greens, broccoli, and asparagus), citrus fruits, whole grains, wheat germ, avocados, dried beans, and peas.

MINERALS

WHY ARE MINERALS IMPORTANT FOR YOUR HEALTH?

Minerals are required by the body for all aspects of life. Their major functions are to form the structural elements of the body and to speed up enzymatic reactions. Some minerals are required in relatively large amounts, while others are only needed in ultra-trace quantities. Since the body cannot produce its own minerals, they must be provided through food sources or supplementation.

CALCIUM

WHY IS CALCIUM IMPORTANT FOR YOUR HEALTH?

Calcium is vital for the development and strength of bones. The body typically contains 2 to 2.5 pounds of calcium, about 99 percent of which is locked up in bones and teeth. The remaining one percent, found in the blood and soft tissues, is essential for life and health, including proper muscle contraction, blood clotting, and nerve impulse transmission. The body continually tears down and rebuilds bone to make calcium available for our vital functions. If we don't get enough calcium from food, the body automatically takes the needed calcium from the bones. When the body continues to tear down more bone than it replaces over a period of years to get calcium, the bones become weak and fragile. This weakness can potentially lead to a crippling bone disease called osteoporosis. Approximately 28 million American women and men have some degree of osteoporosis. This is particularly common in women after menopause.

TIPS AND ADVICE

- Dietitians and nutritionists recommend adult men and women consume 1,000 milligrams of calcium daily.
- One cup of milk or eight ounces of yogurt each contain 300 milligrams of calcium.
- Adding dry milk to stews, soups, gravies, and sauces (1/4 cup) provides 375 milligrams of calcium—a big jump to meeting daily needs.

FOOD EXAMPLES

Milk and foods made from milk are the richest dietary sources of calcium. It may be difficult to meet the daily requirements for this mineral without dairy products. However, calcium is also found in dark green vegetables, nuts, canned salmon and sardines (if you eat the bones), tofu (set in calcium), and calcium-fortified foods and beverages.

MAGNESIUM

Magnesium is needed for the function of more than 300 different enzymes and is critical for the performance of the healthy cardiovascular system. However, the average U.S. diet supplies only about sixty percent of the recommended daily intake of this key mineral.

FOOD EXAMPLES

Rich sources of magnesium are dark green vegetables and nuts.

POTASSIUM

Potassium is one of the most abundant minerals in the body. Among its other functions, it is involved in maintaining normal heart rhythm and regulating the body's water balance.

FOOD EXAMPLES

Most fruits and vegetables are good sources of potassium.

SELENIUM

Selenium has a variety of functions. The main one is its role as an antioxidant in conjunction with glutathione. It also enhances vitamin E function and has been shown to improve the production of sperm and sperm motility. Selenium is a co-factor in thyroid hormone metabolism.

FOOD EXAMPLES

Selenium is found in organ meats (such as liver and kidney), oysters, tuna, herring, whole grains, nuts, brewer's yeast, wheat germ, and vegetables. The amount of selenium in vegetables depends on the selenium content of the soil.

ZINC

Zinc is needed for the function of more than 80 enzymes. It is critical for a healthy immune system, digestion, protein formation, skin integrity, and the performance of antioxidant enzymes.

FOOD EXAMPLES

Meat, liver, eggs, seafood (oysters), and vegetables are all great sources of zinc.

CRUCIFEROUS VEGETABLES

WHY ARE CRUCIFEROUS VEGETABLES IMPORTANT FOR YOUR HEALTH?

Cruciferous vegetables contain substances called glucosinolates and, according to the latest medical research, glucosinolates offer protection against certain illnesses such as cancer and heart disease. These vegetables activate detoxification enzymes, helping your body remove toxins.

TIPS AND ADVICE

- Avoid overcooking cruciferous vegetables so as not to lose the vitamins, minerals, and special compounds these vegetables contain.
- All cruciferous vegetables are ideal for a stir-fry, which allows them to retain their color, crunchiness, and unique flavor. They can also be lightly steamed.
- Whenever possible, eat these vegetables raw; cut them up and serve with a dip.

FOOD EXAMPLES

The cruciferous vegetables are so named for their cross-shaped flowers. A major subgroup is the Brassica, which includes cabbage, brussel sprouts, broccoli, cauliflower, kale, kohlrabi, turnips, and watercress.

ALLIUM VEGETABLES

WHY ARE ALLIUM VEGETABLES IMPORTANT FOR YOUR HEALTH?

Much like cruciferous vegetables, allium vegetables aid the body's detoxification systems. These vegetables also contain antioxidants, which help remove destructive molecules called free radicals that have been implicated in aging and in a variety of illnesses. While all allium vegetables are beneficial for your health, most research has focused on garlic. According to latest research, among its other effects, garlic appears to reduce the risk of cancer and prevent thrombosis, a dangerous blood clot formation.

TIPS AND ADVICE

- Garlic and onions lose much of their effectiveness during cooking. Eating these vegetables raw or very lightly cooked is always best.
- Garlic can be taken in a supplement tablet, but it is always preferable and more effective to eat fresh garlic. The presence of the distinctive garlic aroma is a good indication of its effectiveness.
- The American Institute for Cancer Research recommends you eat a minimum of two to five cloves of garlic a week.

FOOD EXAMPLES

Allium vegetables include onions, spring onions, green onions, chives, shallots, garlic, and leeks.

OMEGA-3 FATTY ACIDS

WHY ARE OMEGA-3 FATTY ACIDS IMPORTANT FOR YOUR HEALTH?

A number of studies have shown omega-3 fatty acids to be protective against cardiovascular disease. These benefits include a reduction in plasma triglycerides, blood pressure, platelet aggregation, and inflammation. New research also shows omega-3 fatty acids can help increase bone formation and reduce bone re-absorption.

TIPS AND ADVICE

Plan to eat at least two to five servings of fish a week. When choosing a fish for a meal, try to include the types with the highest oil content. If you are unable to get enough omega-3 fatty acids through diet alone, you may consider taking a high quality supplement.

FOOD EXAMPLES

Oily fish such as herring, salmon, mackerel, trout, and sardines are the richest sources of omega-3 fatty acids and other fish, including cod, halibut, catfish, flounder, and canned tuna, are moderate sources. Among shellfish, oysters have high levels of omega-3 fatty acids, and shrimp, crab, and scallops have moderate levels. Additional sources of omega-3 fatty acids are flaxseed oil, canola oil, soybean oil, walnut oil, flaxseeds, and walnuts.

CARBOHYDRATES, GLYCEMIC LOAD (GL), AND GLYCEMIC INDEX (GI)

WHAT IS GLYCEMIC LOAD AND GLYCEMIC INDEX?

Carbohydrates serve as one of the body's two main sources of energy (the other is fat). How your body responds to the various carbohydrates in foods depends on the foods' Glycemic Index (GI). The GI is a ranking of carbohydrate-rich foods on a scale from 0 to 100 according to how much they raise blood glucose levels after eating. High GI foods are rapidly digested and absorbed, which may result in large swings in blood glucose levels. Low GI foods are digested and absorbed more slowly, and may result in more stable levels of blood glucose. Glycemic Load (GL) takes into account the GI of a food and the amount of the food that you eat to measure the full impact on your blood glucose levels. The higher the GL, the greater the increase in blood glucose. For long term health, it is best to consume foods with a lower GL to decrease the fluctuations in blood glucose and promote optimal health.

TIPS AND ADVICE

- Consume whole grains. The fibrous coat of the hull or skin slows down the digestion and absorption of carbohydrates. An example is brown rice instead of white rice.
- Choose brown long-grain rice as it has the lowest GI compared to other rice. Eat breads with a lower GI, such as rye bread or any whole grain variety.
- Pasta has a low GI but a large portion will result in a high GL.
- Include legumes such as beans and peas in your diet, they are the mainstay of a low GI diet.
- Don't overcook carbohydrates. Extensive cooking causes the starch fibers to break down, making them easier and faster to digest.
- Avoid sugary beverages such as fruit juices and soda and minimize sugary/refined cereals, candy, and desserts.

FOOD EXAMPLES

Low GL Foods:
Bran cereals, apples, carrots, chick peas, grapes, green peas, sweet corn, strawberries, pinto beans, watermelon, cantaloupe, red lentils
Medium GL Foods:
Apple juice, wild rice, bananas, sweet potatoes, sourdough wheat bread, sweet potatoes, shredded wheat
High GL Foods:
Bagels, corn flakes, white rice, potatoes, spaghetti, couscous, sugar

SATURATED FATS

HOW DO SATURATED FATS AFFECT YOUR HEALTH?

Fats provide us with a concentrated form of energy. They supply essential fatty acids the body itself cannot produce, help the body store energy, insulate tissues, and absorb fat-soluble vitamins and hormones. Fats are divided into two main groups: saturated and unsaturated. Saturated fats can raise LDL, or "bad" cholesterol levels. High LDL cholesterol has been linked to cardiovascular disease. Other fats to avoid are trans fatty acids because they can also increase the "bad" LDL cholesterol and lower the "good" HDL cholesterol. In contrast, unsaturated fats do not increase blood cholesterol and may in fact decrease it.

TIPS AND ADVICE

- U.S. Health authorities recommend individuals get less than thirty percent of their total calories from fat and less than ten percent of their total calories from saturated fats.
- Prepare food with the minimum amount of fat by choosing grilling, baking, steaming, poaching, and stir-frying over frying and roasting.
- Choose vegetable oils (such as olive or canola). Use avocado oil over butter, lard, or cream.
- Avoid margarines that contain hydrogenated fats and trans fatty acids (check the packaging labels).
- Buy lean meat, poultry, and pork. You can also remove any meat fat yourself before cooking.
- Read food labels to check for fat content. A low-fat product should contain no more than five grams of fat per 100 grams of food, and preferably no more than ten grams of fat per portion.

FOOD EXAMPLES

Saturated fats are found mainly in animal foods, and are usually solid at room temperature. Foods high in saturated fats include high-fat dairy products (such as cheese, whole milk, cream, butter, and ice cream), processed meats, the skin and fat of poultry, and lard. Palm oil and coconut oil are also saturated. Trans fatty acids are often found in prepared foods. Examples are brick or block margarines, shortenings, cookies, and other baked goods. Unsaturated fats are liquid at room temperature and are found in vegetable oils, nuts, olives, avocados, and fatty fish.

CHOLESTEROL

HOW DOES CHOLESTEROL AFFECT YOUR HEART HEALTH?

Cholesterol is a substance our bodies need to function normally. However, if there is too much cholesterol in your body, it can lead to the development of cardiovascular disease and stroke. Almost 500,000 Americans die annually from coronary heart disease. Physicians distinguish between two forms of cholesterol. The so-called "bad" (LDL) cholesterol may increase the risk of disease. Our blood also contains another form, referred to as "good" (HDL) cholesterol, which protects us against arterial disease. Therefore, it's important to have not only normal blood cholesterol levels, but also a healthy ratio between "bad" and "good" cholesterol.

TIPS AND ADVICE

- Contrary to popular belief, most cholesterol in the blood is manufactured by the body itself.
- The foods with the strongest impact on cholesterol levels are saturated fats. Foods rich in cholesterol and trans fatty acids can also increase blood cholesterol, although to a lesser extent.
- Fiber has been shown to decrease total cholesterol and increase the "good" cholesterol. In particular, soluble-fiber foods such as oat bran and oats are among the finest foods for combating high cholesterol levels.
- The American Heart Association recommends a healthy diet should contain no more than 300 milligrams of cholesterol daily.

FOOD EXAMPLES

Dietary cholesterol is found only in animal foods such as egg yolks, dairy fats, organ meats, beef, chicken, and shellfish. Vegetable oils and shortenings are cholesterol-free.

CAFFEINE

HOW DOES CAFFEINE AFFECT YOUR HEALTH?

Caffeine is a mild stimulant that affects the central nervous system. Most Americans regularly consume caffeine in drinks, food, or medications, such as certain pain relievers and flu medicines. While a moderate amount of caffeine is usually harmless, in some people, excessive caffeine can cause anxiety, insomnia, headaches, or stomach irritation. Excessive caffeine can be bad for bone health as it can prevent the absorption of vitamins and minerals, including the ones that build up bone, such as calcium.

TIPS AND ADVICE

- According to the U.S. Department of Agriculture and the National Coffee Association, each six-ounce cup of brewed coffee contains approximately 100 milligrams of caffeine. The current recommendation is not to exceed 300 milligrams of caffeine a day.
- It is important to take into account all of your caffeine sources throughout the day. This includes your consumption of coffee, tea, chocolate, cola, and energy drinks.
- To cut down on caffeine, substitute herbal tea, hot cider, or decaffeinated coffee for caffeinated drinks.
- Be aware and read labels: caffeine is an ingredient in more than 1,000 over-the-counter and prescription drugs.

FOOD EXAMPLES

Drip coffee has the highest concentration of caffeine (115–135 milligrams per cup). Other common caffeine sources include espresso (100 mg per 2 oz), tea (40-60 mg), soft drinks (35-55 mg per 12 oz), and chocolate (10-30 mg per 1.5 oz).

PHYSICAL ACTIVITY

HOW DOES PHYSICAL ACTIVTY AFFECT YOUR HEALTH?

Regular low-moderate intensity endurance exercise can give you a plethora of health benefits and reduce the risk of premature death from preventable diseases. Activity need not be strenuous to have a beneficial impact on health. U.S. health authorities recommend that all adults get at least 30 minutes of moderate physical activity preferably every day.

TIPS AND ADVICE

- See attainable and achievable goals. Do not set yourself the target of running a marathon if you have done no exercise for the last decade. Set yourself achievable goals so that you will feel satisfied when you overachieve rather than risk underachieving. Reassess your goals regularly to ensure you are still working hard enough as your fitness improves. Tell your friends and family so they can encourage you to keep exercising if your enthusiasm starts to wane.
- Be realistic, if you are overweight then start with gentle swimming or walking and then gradually build up. Before long you will be doing far more than you ever imagined.
- Find an exercise partner; you can help motivate each other as well as keep each other company while exercising.
- Invest in appropriate equipment for your chosen exercise mode. A good pair of training shoes appropriate for the type of exercise may prevent injury and add enjoyment to your chosen activity.
- Try to vary the type of exercise that you do so that you keep exercising for life and not drop it after a few weeks. The most popular types of exercise are walking, running, hiking, cycling, rowing, swimming, dancing, and aerobics. If you are not fit enough to jog, then start with walking and gradually increase your pace and distance until you are fulfilling the recommended amount for health benefits.

PRECAUTIONS

Before beginning any exercise program that includes vigorous exercise, the following individuals should have a medical examination by a physician.

- Men over 40 years of age
- Women over 50 years of age
- People at high risk or who have familial history of coronary heart disease e.g., Individuals with high blood pressure, obesity, diabetes, or high cholesterol
- If you are in any doubt of your state of health then be sure to consult with a physician before commencing on your exercise regime

FREQUENTLY ASKED QUESTIONS

HOW CAN UNDERSTANDING YOUR GENES GIVE YOU A LONGER, HEALTHIER LIFE?

Your health is a result of interactions between your genes and lifestyle factors such as diet, exercise, stress, smoking, and alcohol consumption. It is your genetic makeup that determines which nutrients are used and how they are used, the way toxins are removed, and how effective these key processes are within the body. However, by adjusting your lifestyle, you can have a great impact on how your genes work and compensate for areas in which your genes are functioning at an altered level.

DOES THE GENE TEST OFFER ANY BENEFIT THAT I WOULDN'T GET IF I FOLLOWED ALL THE GOOD ADVICE FROM HEALTHCARE PROFESSIONALS, RESEARCH ORGANIZATIONS, MAGAZINE ARTICLES, SPECIALIZED HEALTHCARE CHARITIES, ETC.?

Today, every pharmacy, health food shop, magazine, and supermarket is stacked with dietary and nutrition advice, much of it sound and healthy. But how do you know which guidelines are relevant for you? Besides, the problem is not only the quality but the quantity—it's too much for anybody to take in. Little wonder that according to U.S. government surveys, only twelve percent of Americans comply with the general guidelines for healthy eating. In contrast, focusing on personal advice—specific guidelines tailored to your particular needs—is much more realistic. Our experience shows that personal advice provides people with that extra bit of motivation for making a stronger commitment to healthy living.

WHAT KIND OF GENETIC SCREENING DOES THE TEST INCLUDE?

The screen focuses only on gene variations that may call for changes in diet or lifestyle. By learning about the specific nature of some of your genes from your report, you will learn to focus on factors that could be of greatest benefit to your health. Our DNA analysis does not include genes that do not interact with your nutrition or lifestyle.

CAN YOU TELL ME IF I CARRY THE GENES FOR A SERIOUS, INHERITED ILLNESS?

No, our screening is not a test for inherited disorders or inherited predisposition to disease. We do not screen for disorders caused by a defect in a single gene, such as Huntington's disease, cystic fibrosis or sickle cell anemia. We do not test for inherited genes linked to a specific disease—for example, genes associated with certain forms of breast cancer that run in families. People with a family history of such relatively rare illnesses are likely to already be receiving counseling and support within the healthcare system. If you think you may carry the genes for an inherited disease, you should speak to your doctor.

Our screening process is relevant only for the much more common situation: the presence of gene variations that influence a person's ability to derive maximal benefit from diet and lifestyle practices recommended by current medical research for maintaining health and well-being. While we cannot promise that if you take our advice you will never become ill, we provide you with direction and guidance that allows you to make informed choices about your diet and lifestyle that give you a better chance of staying well.

WILL YOU BE ABLE TO TELL ME IF I'M ILL?

No, we can only determine what types of genes people have and how they relate to certain metabolic factors involved in well-being. Specifically, we analyze 19 genes that have an impact on bone health, antioxidant/detoxification, inflammation, heart health, and insulin sensitivity.

ARE GENE VARIATIONS A CAUSE FOR CONCERN?

Most of the time, gene variations have no effect on our body systems or our health, and in certain cases these variations can even be beneficial. However, sometimes a variation can make the gene send a slightly altered message to the cell. Upon receiving the altered message, the cell will manufacture a product—such as an enzyme—that doesn't work exactly as it should; the variant enzyme may, for example, work faster or slower than is best for the body. Combined with an unhealthy diet or lifestyle, such a gene variation may have a negative impact on health and well-being. By following advice that takes into account the presence of genetic variations, you can increase your chances of maintaining good health.

WILL ANYONE OUTSIDE YOUR COMPANY HAVE ACCESS TO MY DNA RESULTS OR QUESTIONNAIRE?

No. All of the personal information you chose to share with us (your DNA sample, your identifying details, and personal health information) is kept strictly confidential. We are aware of the need for strong and appropriate privacy safeguards, and that is why we ensure that no one has access to your information without your prior consent. We "de-identify" the material you send us to make sure that your identity is separate from your information that undergoes evaluation. We do not sell information or disclose any details to third parties, such as insurance companies. There is a label on your DNA sample and your DNA is identifiable only by that label, and even members of our lab staff do not know to whom the sample belongs. When the analysis has been completed, the sample is physically destroyed. We do, however, keep your contact information separately in our databases for further communication with you.

WILL YOU LOOK AT MY COMPLETE GENOME?

No. The Human Genome Project, involving an international network of research centers over many years, has recently accomplished a monumental task: deciphering the three billion "letters" of the human genetic code. Scientists are currently tackling the next frontier: understanding how these genes work and what functions they perform in the body. However, for most genes, such an understanding is still years away. At present, deciphering a person's entire genome—even if this were realistic—would not be particularly useful. However, genetic science has already yielded sufficient knowledge to have an impact on our daily lives: an understanding of how gene variations affect the way our bodies process certain nutrients. What's unique about our service is that by analyzing these variations, it allows people to know enough about their genetic makeup to adopt a healthier lifestyle.

IS YOUR COMPANY INVOLVED IN SUCH AREAS OF GENETIC RESEARCH AS CLONING, GENETICALLY MODIFIED (GM) FOODS OR GENETIC ENGINEERING?

We conduct research, both in our own laboratories and in partnership with leading universities, to explore the relationship between genetics and health. Our research focuses on providing personalized lifestyle advice. We do not carry out research into cloning, and we are not engaged in the genetic manipulation required to produce GM foods or other genetically engineered products. We do not engage in any research that involves the use of animals.

WHAT SHOULD I DO IF I HAVE QUESTIONS ABOUT MY RESULTS OR REQUIRE FURTHER INFORMATION?

If you have any questions regarding any aspect of our service, please contact us at 1-866-442-4380 from 8am to 4pm (Mountain Time), or by email at info@sciona.com. You can also find more information by visiting our website at www.sciona.com.

WHERE DO I TURN FOR FURTHER NUTRITIONAL COUNSELING?

If you would like to receive further nutritional guidance after reading your personal report, you should consult a dietitian, a nutritionist or your doctor. This may be particularly valid if you have been diagnosed with a food intolerance, an allergy, any medical condition, or if you simply wish to continue learning about healthy eating and lifestyle habits. This report includes a Resource Directory, which lists a number of associations that will refer you to a dietitian or nutritionist in your area.

KEY TERMS EXPLAINED

Allicin – A phytochemical found in garlic that provides health benefits including stimulation of the immune system.

Amino Acid – The basic building block of proteins. Each protein consists of a different set of amino acids, put together according to instructions in the corresponding gene. There are 22 amino acids, each encoded by a three-letter "word" of the genetic code.

Antioxidant – Any compound that prevents or neutralizes the damaging effects of free radicals—reactive oxygen molecules in cells. Some natural antioxidants are produced in the body while others, such as certain vitamins, are found in a variety of foods.

Carbohydrates – Organic compounds that contain carbon, hydrogen, and oxygen. They include simple sugars such as fructose and glucose, as well as the more complex saccharides such as lactose, starch, and cellulose. Carbohydrates are an excellent source of energy and of many vitamins and minerals.

Cell – The basic structural subunit of any living organism. It is a tiny, watery compartment filled with chemicals containing a complete copy of the organism's genome. Some organisms are made up of only one or two cells, whereas the human body consists of billions. Each cell is enclosed by a membrane and in most cases has a nucleus containing genetic material (DNA) organized in the form of chromosomes.

Chromosome – A tightly coiled microscopic structure made up mainly of DNA. Chromosomes are found in most cells of the human body, inside the nucleus.

Cloning – The process of making an identical copy of something. The term is used when making copies of a piece of DNA, usually a gene (molecular cloning), culturing cells (cell cloning) or making copies of a living organism (for example, animal cloning).

Detoxification – The process by which the body rids itself of unwanted and potentially harmful substances, or toxins. These toxins can come from food, water, air, or from the by-products of normal metabolism. Detoxification generally happens in the liver or kidneys, where toxins are either broken down or attached to a water-soluble, natural chemical to be easily excreted in the urine or sweat.

DNA – The genetic material of living organisms, an abbreviation for deoxyribonucleic acid. The DNA is known as a "double helix" because its molecules have the shape of a twisted ladder consisting of two intertwined coils. DNA forms the genetic blueprint; it contains the genes that carry all the information about our appearance, how our bodies function and, sometimes, the diseases we will get. The building blocks of DNA contain four different chemicals—adenine, thymine, cytosine, and guanine, or A, T, C, and G for short—referred to as the "letters" of the genetic code.

Enzyme – A protein that carries out the biochemical reactions essential for the body to metabolize food and produce energy for growth, repair, and movement. Organisms could not function if they had no enzymes.

Fats – Organic compounds, composed of glycerol and fatty acids, that serve as the most concentrated source of energy in foods. Depending on the predominant type of fatty acids they contain, they are divided into saturated and unsaturated molecules.

Free Radical – A reactive molecule that contains an unpaired electron. Free radicals are formed in the body as part of normal metabolism. If produced in excess, or not neutralized efficiently, free radicals can react with and damage proteins, lipids, and DNA in the body.

Gene – A segment of the DNA molecule that contains instructions for making a protein. The sequences of genetic "letters" (e.g., ATT CGG) in our genes determine how, when, and where our bodies make each of the many thousands of proteins required for life.

Gene Variation – A naturally occurring variation in the DNA that is present in at least one percent of the population. The variation means an alteration in one or more letters of the genetic alphabet. For example, where most people have the genetic letter A, the person with the variation may have a T. Scientists call such variations "polymorphisms." Most gene variations are harmless and are part of normal human genetic diversity.

Genetic Code – The instructions in a gene that tell the cell how to make a specific protein. A, T, C, and G are the "letters" of the genetic code; they stand for the chemicals adenine, thymine, cytosine, and guanine, which make up DNA. Each gene's code combines the four chemicals in various ways, spelling out three-letter "words" that specify which amino acid is needed at every step in making a protein.

Genetic Disease – Any disorder caused by defects in genes. Single-gene disorders, which are relatively rare, are caused by mutations in a single gene—for example, cystic fibrosis or sickle cell anemia. More common are complex, or multifactorial, diseases, arising from variations in several genes together with environmental factors. Examples of complex diseases include most types of cancer, heart disease, and diabetes.

Genetic Engineering – The use of various experimental techniques to produce DNA that contains new or modified genes or combinations of genes.

Genome – The total genetic code of a particular organism. The normal human genome consists of about three billion genetic "letters."

Genomics – A specialized branch of science that studies the genome.

Glycemic Index (GI) – A ranking of carbohydrate-containing foods, based on the food's effect on blood glucose compared with a standard reference food's effect.

Glycemic Load (GL) – Glycemic Load is equal to the GI of a food times the number of grams of carbohydrates in the serving of food. Glycemic Load is believed to give a better indication of the changes in the levels of blood glucose than grams of refined carbohydrates eaten.

GM Foods – Genetically modified (GM) foods have been produced using genetic engineering to modify, insert, or remove one or more genes from the genome.

Metabolism – The natural process by which all living organisms, including humans, transform food into energy and dispose of their waste products. Metabolism is essential for life.

Molecule – The smallest part of any compound or substance that is chemically stable. It consists of two or more atoms joined together by chemical bonding.

Nucleus – The central cell structure; it contains the chromosomes.

Oxidative Stress – A situation in which the environment within cells becomes highly "oxidized"—that is, comes to contain reactive, unstable molecules, particularly those of oxygen. These reactive molecules can overwhelm antioxidant defenses and damage cellular proteins, lipids, and DNA. Cells in this highly activated state lose control of their regulatory systems. Oxidative stress has been linked to the development of disease.

Phytochemicals – Natural compounds found in plant foods that have many health benefits including antioxidant effects, stimulation of the immune system, modulation of hormone metabolism, and antibacterial and antiviral effect.

Polymorphism – Scientific term for "gene variation."

Proteins – Complex, organic compounds that contain carbon, hydrogen, oxygen, and nitrogen. It is the presence of nitrogen that differentiates proteins from carbohydrates and fats. The basic building blocks of proteins are amino acids. Humans need 22 amino acids for the synthesis of their proteins. The human body can make only 13, known as nonessential amino acids because we don't need to get them from the food we eat. There are nine essential amino acids that are not made by the body and can be obtained only from food.

SNP – Single nucleotide polymorphism, pronounced "snip." A gene variation that consists of alteration in a single genetic "letter," or base: for example, GGT instead of GCT. Such common, though minute, variations occur in human DNA at a frequency of one in every 1,000 bases.

Toxin – A harmful substance, specifically one produced by an animal, plant, or bacterium. Toxins can enter the body from one of these sources or be generated as by-products of metabolism. Constant exposure to toxins can overwhelm the body's detoxification mechanisms and lead to disease.

Vitamins – Organic molecules that are essential for normal metabolism, growth and development, and for the regulation of cell function. Some vitamins activate specific enzymes in the body. Insufficient vitamins in the diet lead to deficiency.

POPULATION FREQUENCY CHART

Gene	Var	Percentage of Population with Gene Variation						
		Total Frequency*	African American	Asian	Caucasian	Hispanic/Latino	Japanese	Chinese
MTHFR	C677	28.7	10.0	21.1	28.9	47.1	40.3	33.3
MTHFR	A1298C	30.0	25.0	19.2	33.9	17.5	36	14.6
NE MTRR	A66G	47.3	27.5	28.9	52.5	44.1	31.8	20.5
MTR	A2576G	17.4	32.5	7.9	15.8	14.7	18.5	10.4
CBS	C699T	28.0	20.0	2.6	30.0	32.4	ND	4.3
HSOD5	C-28T	54.2	64.6	<1	53.4	65.2	12	67.7
SOD3	C760G	<3	<3	<3	<3	<3	<3	<3
IL-6	G-174C	36.3	<1	<1	47.5	21.9	<1	<1
IL-6	G-634C	10.3	15.0	63.2	5.6	14.7	22.0	ND
TNF-a	G-308A	16.5	12.5	7.9	15.8	26.5	2	2
APOC3	C3175G	12.6	7.5	31.6	13.2	8.8	32.6	29.8
CETP	G279A	37.0	18.4	36.8	40.0	38.2	40	35.4
LPL	C1595G	9.9	7.5	13.2	7.5	23.2	14	6.5
eNOS	G894T	35.6	22.5	15.8	42.5	17.6	12.5	9
ACE	I/DD	61.0	63.6	77.8	57.9	70.0	62	65
GSTM1	Gene Deletion	69.0	32.0	43.0	50.0	47.0	54.5	50.4
GSTP1	A313G	34.8	52.5	28.9	32.5	32.4	27.5	15.2
GSTP1	C341T	11.5	<1	<1	15.8	2.9	<1	2.0
GSTT1	Gene Deletion	21.9	26.0	80.0	20.0	11.0	48.3	45.4
VDR	Taq I	70.6	62.5	92.1	72.5	61.8	14	4.2
VDR	Bsm I	69.6	65.0	89.5	72.5	53.1	23.3	89.35
VDR	Fok I	63.8	65.0	55.3	65.0	58.8	67	46.7
COL1A1	SP1 G>T	21.0	7.5	<1	27.5	5.9	<1	<1
PPARγ2	Pro12Ala	10.3	5.0	2.6	12.5	5.9	3.0	6.2

* Population frequencies given in this column are normalized for the U.S. population data from the U.S. 2002 Census Report. Population frequencies can vary for different ethnic groups as outlined in the subsequent columns.

RESOURCE DIRECTORY

NATIONAL DIETETIC ASSOCIATIONS
American Dietetic Association (ADA)
Tel: 800-877-1600
http://www.eatright.org

Dietitians of Canada
Tel: 416-596-0857
http://www.dietitians.ca

MEDICAL ASSOCIATIONS
American Institute for Cancer Research
Tel: 800-843-8114
http://www.aicr.org

American Diabetes Association
Tel: 800-342-2383
http://www.diabetes.org

NATIONAL HEALTH AND RESEARCH ORGANIZATIONS
U.S. National Institutes of Health (NIH)
Tel: 301-496-4000
http://www.nih.gov

U.S. National Human Genome Research Institute
Tel: 301-402-0911
http://www.genome.gov

U.S. Centers for Disease Control and Prevention (CDC)
Tel: 800-311-3435
http://www.cdc.gov/genomics

Healthfinder®
http://www.healthfinder.gov

RESEARCH CENTERS
A listing of research sources for nutrigenomics and related studies:

University of California at Davis
http://nutrigenomics.ucdavis.edu

Sciona, Inc.
http://www.sciona.com

Centre For Human Nutrigenomics
http://www.nutrigenomics.nl

Institute of Food Research
http://www.ifr.bbsrc.ac.uk

University of Guelph
http://www.uoguelph.ca

NuGO - European Nutrigenomics Organisation
http://www.nugo.org

Tufts University
Jean Mayer USDA Human Nutrition Research Center on Aging
http://www.hnrc.tufts.edu

FURTHER INFORMATION
Book resource:

It's Not Just Your Genes
http://itsnotjustyourgenes.com

Sciona Response to GAO Report 06-977T

Rosalynn Gill-Garrison, Ph.D.
Chief Science Officer
Sciona, Inc.
August 11, 2006

Sciona is pleased to respond to the GAO report "Nutrigenetic Testing" released to the press on July 26, 2006 and released to the public on July 27, 2006. Our company and others have expressed our disappointment that we were not given a copy of the report prior to the hearing of the Senate Special Committee on Aging on July 27, 2006, as the report was the basis of the hearing. At the time of this writing, October 3, 2006, the supporting materials, including the scope and methodology described on the summary page of the report, are not available on the website as listed: www.gao.gov/cgi-bin/getrpt?GAO-06-977T, only a copy of the report is present at this site.

Sciona believes that we are the company from website number 3 described in this report.

Sciona finds the information contained within the report inaccurate and disingenuous. Additionally, Sciona finds the analysis severely flawed. The report centered on the following themes:

1. Allegations of medical claims contained within the report, juxtaposed with criticisms of language used to describe specific gene-diet or gene-environmental relationships.
2. A misunderstanding of the use of the Lifestyle Questionnaire to provide personalized feedback to the individual, in the context of goals for particular nutrition or lifestyle changes due to a particular genetic profile. This misunderstanding is used to claim that the tests are inaccurate.

1. Allegations of medical claims

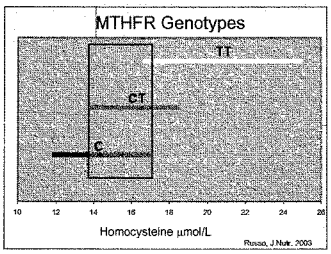
GAO statement:
Although there are numerous disclaimers indicating that the tests are not intended to diagnose disease, all 14 results predict that the fictitious consumers are at risk for developing a range of conditions . . . GAO -06-977T Summary, page 5

Sciona response:
Our reports do not diagnose any disease, as correctly identified in our disclaimers. Sciona does identify particular health conditions associated with particular genetic variations that can be modified by dietary or lifestyle interventions. Within the report, the GAO repeatedly attempts to link diagnosis of disease, which we do not do, with explanations of impacts on health parameters, such as cholesterol levels, homocysteine levels, which we do indeed discuss within the information that we provide to a consumer.

GAO statement:
For example, many people "may" be "at increased risk" for developing heart disease, so such an ambiguous statement could relate to any human that submitted DNA.
GAO-06-977T- Summary page, pages 5,7,8,13,14,15

Sciona response:
The language that we use in our reports complies with FDA guidelines on permitted claims for particular foods. The FDA has provided model claim statements for foods: "While many factors affect heart disease, diets low in saturated fat and cholesterol may reduce the risk of this disease."
GAO-06-977T Summary, pages 6,14,17

The genes that Sciona screens are neither predictive nor diagnostic of a particular disease. There are genes in which a particular mutation is considered diagnostic of a particular disease; cystic fibrosis and Huntington's chorea are two examples of such diseases. However, in biology, these cases in which genes alone determine an outcome are considered the exception, rather than the rule; many diseases are in fact the result of a complex interplay of environment and genetic background, where each factor plays a significant role in the development of health conditions. Sciona's product is focused on specific gene-diet or gene-environmental relationships in which the genetic background and the nutritional or lifestyle choices of the individual have an impact on particular factors such as homocysteine levels or cholesterol levels in the blood stream. Thus, our products cannot be and are not predictive or diagnostic of a particular disease, as the GAO report alleges. Furthermore, the presence of the particular variation does not necessarily mean that each individual will respond in the same way. For example, in Figure 1 below (presenting data from the Framingham population), the MTHFR gene was genotyped and homocysteine levels were measured. What is apparent is that individuals have homocysteine levels that can be grouped according to genotype, but which fall into a range. A person with a CT genotype at position C677T may have homocysteine levels above 15μmol/l, but they may not. Furthermore, the identification of high homocysteine levels, while considered a risk factor in an individual, is not considered diagnostic of heart disease, with or without the use of a genetic test.



2. Misunderstanding of the role of the Lifestyle Questionnaire in providing personalized feed back to the individual.

GAO statement:
In addition, results from the tests that GAO purchased from Web sites 1, 2, and 3 do not provide recommendations based on a unique genetic profile as promised, but instead provide a number of common sense health recommendations.
GAO-06-977T Summary, pages 6, 10,18,19,20

Sciona Response:
The GAO report repeats this allegation many times in the report, and demonstrates a lack of understanding of the information contained within the report, as well as a selective disclosure of the actual statements used in the report.

Each report is designed to give personal feedback to the individual, based on their questionnaire results, and measured against a set of goals for nutritional and lifestyle factors which are based on the genetic results for that information.

Below is an example of folic acid information taken from a sample report. The estimated current intake is based on the questionnaire results, and the goal is based on the presence of genetic variations which have an impact on folic acid metabolism. The text explains the role of the genetic variations identified in health.

1. B vitamins: folic acid, vitamin B_6, and vitamin B_{12}
Your Genetic Profile indicates you have variations in the B vitamin metabolizing genes included in your Heart Health screen. This makes it very important for you to meet your goals of levels of these vitamins to keep your homocysteine levels low and help promote heart health. Your Diet and Lifestyle Assessment indicates that you are not meeting one or more of your goals of B vitamins in your diet, as shown below. You may wish to use supplements to ensure you meet your goals of B vitamins. We recommend you choose a high quality supplement with USP certification.

Your Estimated Current Intake	330 mcg / day
Your Goal – Folic Acid	800 mcg / day
Your Estimated Current Intake	1.2 mg / day
Your Goal – Vitamin B6	15 mcg / day
Your Estimated Current Intake	7 mcg / day
Your Goal – Vitamin B12	20 mcg / day

The report also criticized advice given to the fictitious consumer on tobacco smoking, alleging that there was no genetic basis to the information given. To the contrary, below is an excerpt from the complete information given within a report, in which both the

lifestyle advice and the underlying genetic factors are fully described. The genes involved in the recommendations include the SOD2 and SOD3 genes, referred to as "antioxidant defense genes"; the biochemical function of the enzymes produced by these genes is the removal of free radicals and other products related to the oxidation reactions that occur in the presence of free radicals. GAO-06-977T Summary, page 6, 19

8. Tobacco
For optimum heart health, we recommend that you quit smoking and avoid passive smoke. You have variations in your antioxidant defense genes, which may reduce your ability to remove the free radicals produced by cigarette smoke. You also have variations in genes involved in blood flow regulation, which can lead to increased blood pressure in the presence of cigarette smoke.

Similarly, a criticism of advice on saturated fats was given, without full disclosure of the information contained within the report, specifically without the discussion of the genetic variations identified in an individual.
GAO-06-977T Summary, page 6, 19

4. Saturated fats
Your Genetic Profile shows variations in genes involved in cholesterol and triglyceride metabolism. According to your Diet and Lifestyle Assessment, you are currently exceeding your goal on levels of saturated fats in your diet. A high intake of saturated fats can have a negative impact on heart health. Maintain your saturated fat intake to less than 7% of your total calories and keep total fat—unsaturated and saturated—to less than 30% of your calories.

Your Estimated Current Intake	34 g / day	Exceeds Goal
Do Not Exceed	16 g / day	

The GAO used 14 different Lifestyle Questionnaires, and received personalized feedback for the 14 fictional consumers. The figures shown in the report, particularly Figures 4 and 5, demonstrate that our reports and personal feedback are accurate and based on the information provided, exactly as designed. It is interesting to note that the GAO chose to identify the information given as "Medical Predictions." It is difficult to understand how the biological description of the effect of a genetic variation on cholesterol metabolism equates to a medical prediction.
GAO-06-977T page 9, 10, 11, 12

The report also described concerns that similar biological effects were described for 2 individuals with different genetic profiles. It is difficult to understand exactly what the report refers to, as the actual reports have not been disclosed. However, it is the case that different genes can have an effect on the same metabolic pathway. For instance, there are 3 genes that are screened by Sciona which are involved in detoxification: GSTM1, GSTT1, and GSTP1. A variation in any of these will lead to information describing variations in genes important for detoxification.
GAO-06-977T page 8,10

The report points out a single discordant result in the laboratory results for the female individual in the ENOS gene. The accuracy rate of the laboratory testing is 99.5%, among the highest in the industry. The female DNA would have been screened 12 times in total, with 24 assays performed per test, generating a total of 216 assays. A single discordant result out of 216, results in an accuracy rate of 99.6%. Furthermore, the negative results for the cat, dog and blank DNA samples are a further demonstration of the accuracy of the genotyping. These animal samples were rejected by the laboratory when results could not be obtained that met the laboratory's quality control criteria. The rejection of the samples demonstrates the specificity and accuracy of the analysis, as the gene sequences and genetic variations measured are not the same in different types of animals.
GAO-06-977T pages 3, 7, 21

Our quality control measures were previously described in the Senate testimony:

> The laboratory work for Sciona is outsourced, and the company maintains close scrutiny on the results and performance of the laboratory testing supplier. Each batch of samples which are run by the supplier includes a set of blinded controls supplied by Sciona for processing. The supplier is not aware of the nature of the blinded samples, and so when the results are supplied back to Sciona, these blinded controls are used as a measure of reproducibility and reliability of the laboratory results. The laboratory supplier also uses internal controls chosen by the supplier, and pass/fail criteria have been set in which both internal supplier controls and Sciona blinded controls must be in concordance before any set of results is cleared for report production.

Additional inaccuracies within the report.

1. Sciona pressured to stop sales of products in the United Kingdom

GAO statement:
During the course of our investigation, we found other information that raises concerns for consumers purchasing these tests. For example, we discovered that Web sites 1, 2, and 3 were in fact selling the same genetic test developed by the same company, and that this company was pressured by consumer groups in the United Kingdom to stop selling the test in that country. The company now sells the same type of test in the United States.
GAO-06-977T pages 5, 6

Sciona response:
Sciona was a target of an anti-genetics pressure group in the United Kingdom. There was no pressure from our consumers to stop selling our products. Sciona actually began selling the Cellf product in the United States in February 2003, almost two years before taking the commercial decision to relocate to the United States. This decision was taken because the majority of sales were to consumers in the United States. It is still possible for customers to purchase the Cellf product in the United Kingdom at this time.

2. The Human Genetics Commission found Sciona's products misleading

GAO statement:
The Human Genetics Commission, the U.K.'s strategic advisory body on developments in human genetics, and GeneWatch UK . . . alleged that the company's tests were misleading because no scientific evidence validated their clinical claims.

Eventually, the tests were subjected to assessment by a team of three experts—a clinical geneticist, a scientist leading a program of research in nutritional genomics, and the chief dietitian of a leading teaching hospital. They published the findings in a detailed report that concluded that there was no value in the genetic tests being offered.
GAO-06-977T page 21

Sciona response:
The U.K. Human Genetics Commission ("HGC") expressed no such allegation that Sciona test was misleading. The Sciona service was assessed by a HGC subgroup who

> "acknowledged that the genes being tested did play an important role in nutrition and metabolism."

The HGC subgroup, though, was not convinced of the "predictive value" of the genetic test. However, the Sciona service is not based on disease prediction but on the role of genes in nutrition and metabolism and the appropriate dietary modifications identified in the scientific literature. The full report of the HGC on direct-to-consumer genetic testing, called "Genes Direct," can be found on their website: www.hgc.gov.uk.

The assessment by a team of experts in the United Kingdom was commissioned by the "Consumers Association," a self-styled consumer protection body. Several months before conducting the test the "Consumers Association" had openly allied itself with an anti-genetic campaign group in a broad campaign to ban direct-to-consumer genetic testing. The impartiality of the report is therefore doubtful.

3. No evidence of scientific substantiation

GAO statement:
None of the results we received contained scientific support to assist the consumer in evaluating their credibility, and there is no evidence to suggest that the tests have been evaluated by independent experts.
GAO-06-977T page 13

Sciona response:
There are links to resources within in the personal report appendix and there is ample information on the Sciona website, including a bibliography of published scientific studies on gene-diet interactions, which support the advice given in the Sciona report. Some resources listed in the back of the report:

- American Dietetic Association (ADA)
- Centre For Human Nutrigenomics
- Institute of Food Research
- U.S. National Institutes of Health (NIH)
- U.S. National Human Genome Research Institute

Conclusions:

A careful analysis of the GAO report 06-977T has revealed flaws in the methodology used to examine reports arising from direct-to-consumer testing, flaws in the analysis of the information contained within the reports, and a trend of selectively quoting information out of context and incompletely to support their allegations.

Sciona concurs with the conclusion of the GAO report that the current regulatory environment provides limited oversight. Sciona has been actively engaged with regulatory experts both in the United States and the United Kingdom. Sciona stands behind our product and service and looks forward to working with the government to develop appropriate standards.

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