

March 1, 2011

Mr. James Swink
Designated Federal Officer
Medical Devices Advisory Committee
Center for Devices and Radiological Health
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Re: Docket No FDA-2011-N-0066

Dear Mr. Swink,

Interleukin Genetics appreciates the opportunity to submit comments to the Molecular and Clinical Genetics Panel of the Medical Devices Advisory Committee in advance of the Panel's upcoming March 8th and 9th meeting to discuss and make recommendations on scientific issues concerning direct to consumer (DTC) genetic tests 76 Fed. Reg. 6623 (Feb. 7, 2011).

Interleukin Genetics was founded in 1987 and currently employs 21 people. The Company has conducted for the past 18 years clinical research to create tests to guide improved management of individuals at risk of certain chronic conditions and tests to improve wellness via proper choice of lifestyle. Our overall mission is to provide tests that can help individuals improve and maintain their health. Our Company sells only genetic tests; we do not sell any other ancillary services, dietary supplements or other products. The Company currently offers five tests. We conduct clinical validity and utility studies on our tests at leading academic institutions throughout the world and with active input from a leading scientific advisory board. Four tests are sold with access by consumers under the Inherent Health brand¹.

Interleukin Genetics believes that direct access to personalized genetic information allows consumers to take greater control of their health. Having individuals empowered to take more preventive measures to maintain good health is in the public interest. We recognize that certain tests have the potential to cause harm whereas others can safely be offered to the public. Further, we believe that all tests, whether ordered and received directly by consumers or solely by health care providers, should meet certain threshold quality and performance measures to ensure analytic and clinical validity.

Given the wide spectrum of genetic tests available² and the great variation in risks and benefits posed by such tests, we believe a "one-size-fits-all" regulatory approach

¹ One of our tests, PST® is sold only via a medical sales force to dentists

² See Human Genetics Commission (HGC), [A Common Framework of Principles for Direct to Consumer Genetic Testing Services: Principles and Consultation Questions 5 \(2009\) \(Table 1\)](http://www.hgc.gov.uk/UploadDocs/DocPub/Document/Principles%20consultation%20final.pdf), available at <http://www.hgc.gov.uk/UploadDocs/DocPub/Document/Principles%20consultation%20final.pdf>

would not be in the best interest of the public. We agree with the views previously expressed by FDA officials, as well as by expert scientific advisory bodies, that oversight of genetic testing should be stratified based on risk. In these comments, we propose criteria for distinguishing between tests that:

- a) should not be allowed to be sold directly to consumers,
- b) may appropriately be available directly to consumers, but only if the information is delivered to a customer by a trained professional, and
- c) should be permitted to be sold directly to consumers without the need for delivery of the information by a trained professional (unless desired by the consumer) but accompanied by information that accurately and clearly explains the results and their potential implications.

Further, we identify core elements that we believe should be included in any regulatory framework for DTC genetic testing. These items are described below.

1. Categorization of Tests Appropriate for DTC Based on Risks and Benefits

- A. Characteristics of Risk Associated with Genetic Testing

The risk associated with a genetic test is derived primarily from a) the intended use as evidenced by the manufacturer's claims, and b) the consequences that may result from the test. Risks can be exacerbated or mitigated by both the accuracy of the test results and how the information is delivered to the recipient.

Thus we believe it is possible to characterize the risk of genetic tests into three categories: "high risk," "moderate risk," and "low risk." This categorization can then be used to define requirements for who may order the test and receive results, the level of scientific evidence needed to support test claims, and how and by whom information should be delivered.

- i. High Risk Genetic Tests

We would define a high risk genetic test as one that provides results that (1) could lead an individual to undertake immediate harmful actions in the absence of guidance by a trained professional, and (2) requires a trained professional with access to the individual's medical and health history or with responsibility for the individual's medical management to interpret and deliver the results.

An example of a high risk test would be a pharmacogenetic test that reports on the individual's drug metabolism or other genetic factors

that influence how a person might respond to a particular medication or dosage. A person obtaining pharmacogenetic information without their physician's knowledge might decide to stop taking or alter the dosing of their medication resulting in a serious adverse event. Even a trained professional cannot adequately provide counseling and guidance regarding the result of a pharmacogenetic test in the absence of access to the individual's medical history, and the advice should be provided by someone who also has responsibility and authority to prescribe medication or the patients and monitor adverse reactions. We therefore believe that pharmacogenetic tests, and other tests meeting the high risk criteria, should not be sold DTC.

ii. Moderate Risk Tests

A "moderate risk" test is one in which there is minimal likelihood for an individual to take actions that would lead to immediate harm when test information is properly interpreted. For these types of tests there is a range of actions and hence a range of medical or psychological consequences in response to understanding the test results. For such tests the genetic information, if properly delivered, would allow for proper action by the customer and does not need other customer-specific medical or family information to be considered. Moderate risk tests may or may not need delivery by a healthcare provider depending on the degree and type of the potential consequences of the particular test.

An example of a moderate risk test requiring delivery of the genetic information by a professional is one reporting the risk of a chronic, untreatable condition (such as Alzheimer's disease). In such case due to potential psychological consequences of receiving the information, delivery of the information would be best if done by a trained healthcare provider. Such Company provided professionals should be able to deliver the genetic information to the customer to provide adequate guidance.

Certain moderate risk tests will not require a healthcare provider as information necessary to interpret the genetic result properly are readily available and understandable. Information on risk and risk reduction for most treatable chronic diseases is available to consumers through government websites³ and academic websites⁴. Documentation properly presented to the customer can enable the customer to adequately interpret the results. A recent study⁵ found that genetic risk information produced minimal negative response from consumers and some positive changes in

³ <http://hp2010.nhlbi.nih.net/atp/iii/calculator.asp>,
http://www.heart.org/HEARTORG/Conditions/HeartAttack/HeartAttackToolsResources/Heart-Attack-Risk-Assessment_UCM_303944_Article.jsp

⁴ <http://www.reynoldsriskscore.org/>

⁵ Cinnamon S. Bloss et al., *Effect of Direct-to-Consumer Genomewide Profiling to Assess Disease Risk*, 364 NEW ENG. J. MED. 524 (2011).

prevention behavior. Such tests should be allowed directly to consumers with a provider counseling needed.

We support direct access by consumers to tests of moderate risk. However, for those tests with untreatable conditions delivery of the information should be conducted by a trained healthcare provider. For moderate risk tests of a treatable and preventable conditions, genetic information communicated concurrently with appropriate, understandable guidance should not require a trained healthcare provider for adequate delivery of the information. Appropriately trained genetic counselors should be made readily available for customers desiring further clarifications.

iii. Low Risk Tests

Finally, tests that are “low risk” would be ones for which there is minimal potential or low likelihood for an individual to take actions that would lead to immediate harm. For low risk tests the reasonable range of actions in response to the test results would have a minimal degree of medical or psychological consequences even if the genetic information were incorrect or misunderstood. An example of a low risk test is a nutrigenetic test that provides information about individual response to certain macronutrients or exercise regimes. Nutrigenetic tests are low risk because a false negative or false positive result that would guide a person to a certain standard diet is not likely to result in negative health outcomes. In addition, misinterpretation of nutrigenetic results by the consumer such as initiating a low-fat diet as opposed to a low carbohydrate diet is also unlikely to cause any serious negative consequences. Given that many individuals already largely make self-directed decisions on diet and exercise without physician supervision the requirement for a trained professional to provide genetic information leading to better weight management is unnecessary.

B. Benefits of Direct Access to Genetic Information

Improved prevention is the key to reducing healthcare costs. We believe that it is important to acknowledge the potential value genetic information may play not only in personalized medicine but also in personalized prevention. A focus on prevention should be an increasingly greater part of the US healthcare system. Research is beginning to show that individuals may benefit from prevention guidance that goes beyond standard public health recommendations. With the decreasing cost and increasing availability of various technologies for assaying large numbers of gene variations, individuals have access to predispositional risk information for several conditions. We support wide access by individuals

to information that will assist them in preventing chronic diseases of aging and improving their health.

For example, we believe that certain nutrigenetic tests, which are intended to provide information about an individual's responsiveness to a particular nutrient or diet, may offer great opportunity for health benefit. A Gallup-Healthways Well-Being Index showed that 63.1% of adults in the U.S. were either overweight or obese in 2009.⁶ New technologies, such as nutrigenetics that can provide individuals with information to improve their weight loss predictability and better manage their weight, are therefore desperately needed. Properly validated nutrigenetic tests can be new tools to guide diet and exercise regimens.

2. Core Elements of a Regulatory Framework

A genetic test provided direct to consumers represents a special circumstance of access to the test, but does not inherently alter either the requirements of quality of the test information.

A. Adequate Scientific Support of Test

We fully support that there must be credible scientific evidence supporting the validity of claims made by any genetic test. However, the amount of scientific evidence necessary to support marketing of a DTC genetic test should be commensurate with the level of risk and the potential degree of benefit that such a test potentially offers. Facilitating market entry of low risk/beneficial tests, while scrutinizing market entry of high risk tests, should be the cornerstones in developing evidentiary standards for genetic testing. At the same time, it is important that pre-dispositional disease risk assessments employ risk calculations based on accepted methodologies for representing risk given the claims of the test. In addition, if combinations of genetic markers are used to characterize risk for a single individual, there should be clinical evidence supporting the value of the specific combination of genetic variants to be reported given the test claims.

B. Laboratory Certification and Analytic Validity

We believe that all commercial genetic tests should be conducted in a laboratory that is certified or accredited by an independent agency or organization and should be able to demonstrate the analytical validity of their tests. The Center for Medicare and Medicaid Services (CMS) regulates all clinical laboratory testing under the Clinical Laboratory Improvement Amendments of 1988 (CLIA).⁷ The objective of the CLIA

⁶ <http://www.webmd.com/diet/news/20100210/percentage-of-overweight-obese-americans-swells>

⁷ 21 U.S.C. § 263a.

program is to ensure quality laboratory testing. Under CLIA regulations laboratories must be inspected in order to assure the quality of the testing process. We fully appreciate the importance of analytic validity for all genetic tests to improve decision making based on the test results. There is a need for verification of laboratory qualifications and test performance parameters. We believe the processes in place by CLIA are adequate to ensure the laboratory quality for genetic tests and should not be replicated in another agency.

C. Improvement is Needed for Reporting of DTC Genome Scanning/Sequencing Information.

DTC genetic testing often refers to the partial genome scans for an individual of several thousand genetic variants. Risk reporting from genome scans are based on an individual company's selection of gene variants and their mathematical calculations via combinations of risk parameters. The test reporting format from scanning is significantly different from report formats from laboratory developed test for a specific single indicated use. Scanning-generated genetic information is provided to customers for numerous conditions and uses simultaneously. Reports generated from partial genome scans may include results and information for high risk, moderate risk and low risk conditions in a single report. As noted above, specific conditions tested may or may not be appropriate for DTC access and may have very different clinical validity evidence requirements. Each intended use should be viewed as an independent test. Requirements for direct access, communication of results, and level of evidence from scans should follow the recommendations noted above based on the type of test being reported. In addition, if a test result is based on a combination of multiple gene variants, there should be clinical evidence validating the specific combination of gene variants used in generating the test result. Finally, the test result for a particular use obtained from these genome scans should disclose the methodology by which the result is calculated to minimize the confusing and conflicting nature of inter-company and even intra-company reports⁸.

D. Proper Consent and Privacy of Genetic Information

We support the main principles regarding protection for the consumers, for example those outlined in the UK Commission's report⁹. These include full disclosure of the limitations of the test, the rights of the individual with regard to use of their DNA samples, a thorough and proper informed consent document, the provision of answers to frequently asked questions, and the availability of a trained genetic counselor to answer questions. In addition, the privacy of genetic information reported in test

⁸ Ng et al. An Agenda for Personalized Medicine. Nature 2009;461:724-6

⁹ See supra note 2.

results must be protected. We also believe that test providers should understand the impact of the type of test when designing their model of test delivery.

E. FDA Registration and Listing

Companies offering DTC moderate and low risk genetic tests that meet the statutory definition of a medical device, 21 U.S.C. § 321(h), should be required to register with FDA and list the tests they offer (each single indicated use reported being defined as a test). No premarket submission should be required for such tests; however, companies should be required to include a disclaimer in labeling for the test that the test has not been reviewed or approved by FDA. If a company seeks to offer the test without including the disclaimer, the company should be required to submit a 510(k) premarket notification submission to FDA. A company must have on file, and make available to FDA on request, information to support a test's analytical validity and clinical claims. We have included for your consideration a summary of potential guidelines for DTC genetic test marketing and reporting (See Appendix A).

Genetic testing is a new science that has potentially great benefit for improving health. Increasing access to new technologies and information that would allow individuals to take greater control of their health management is highly desirable. We support efforts to improving the current situation with regard to direct access of genetic information by consumers. We believe that our proposals provided in this letter benefit consumers with regard to the dissemination of genetic information. Thoughtful consideration; however, must be given to any regulation that would be overly burdensome to the companies innovating in this new scientific area.

Interleukin Genetics appreciates the opportunity to submit these comments for the committee's consideration.

Sincerely,



Lewis H. Bender
Chief Executive Officer
Interleukin Genetics, Inc.

LHB/ms

Appendix A

Proposed direct consumer access genetic tests guidelines

- 1) **DTC Test Registration and Listing.** Companies wishing to market DTC genetic tests must register with FDA and list each genetic test prior to launch. (Existing companies with tests currently on the market should be given one year to list.) Registration should include the following:
 - a. name of test and its intended use,
 - b. classification that identifies the type of risk (low or moderate, since high risk tests should not be permitted to be sold DTC),
 - c. the CLIA lab registration number where the test is being conducted.
- 2) **Definition of a Test.** A test shall be defined as each single intended use reported to an individual in a report. Reporting of conflicting guidance information in a report should be avoided.
- 3) **Delivery of Test Information.** As noted in these comment, certain (but not all) DTC test results should be delivered only by a professional. For tests requiring delivery of information by a trained professional, a Company marketing a genetic test should assure that only qualified/certified professionals (genetic counselors or physicians) are delivering the information to the customer for each test where such information needs professional delivery prior to customer receiving any results.
- 4) **Marketing.** Registered medical tests in low risk and moderate risk categories should be permitted to be marketed DTC, but must include a disclaimer in labeling stating that the test has not been cleared by FDA. Should the provider wish to include a statement that FDA clearance has been obtained, the test provider should be required to submit the appropriate filing documentation (e.g. 510(k)) to FDA. Analytic validity data and scientific data the company possesses supporting the test should be on file and subject to FDA inspection upon request.