July 19, 2015

The Honourable Rona Ambrose, P.C., M.P.
Health Canada
Brooke Claxton Building, Tunney’s Pasture
Postal Locator: 0906C,
Ottawa, Ontario K1A 0K9

Subject: Direct-To-Consumer (DTC) genetic testing in this country

As the voice of Medical Genetics professionals in Canada, we are writing to express our concerns with the lack of legislation pertaining to Direct-To-Consumer (DTC) genetic testing in Canada, and the risks this creates for Canadians and the Canadian healthcare system. **We feel it is imperative that the government promptly establish clear boundaries around DTC genetic testing.**

Tests ordered directly by the consumer, without the involvement of a healthcare provider\(^1\), have become a growing concern in Canada over the last number of years; in particular over the past year. The Health Canada medical device regulation\(^2\) states that “genetic testing means the analysis of DNA, RNA or chromosomes for purposes such as the prediction of disease or vertical transmission risks, or monitoring, diagnosis or prognosis.” In contrast, an “in vitro diagnostic device” or “IVDD” means a medical device that is intended to be used in vitro for the examination of specimens taken from the body.” Despite the fact that most DTC genetic testing companies have been careful about marketing their devices as recreational testing, we believe that DTC genetic testing should fall under this IVDD definition. 23andMe, a prominent player in the field, is actively marketing the health-related aspects of its service to Canadians (www.23andme.com/en-ca).

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While Canada has failed to regulate these tests, the United States (US), through the FDA, has been proactive and categorized the service as a medical device (in vitro diagnostics). As a result, in November 2013, the FDA prohibited 23andMe from marketing health-related claims to Americans given the company’s inability to provide assurance of its test’s analytical or clinical validity. In February 2015, the US FDA granted approval to 23andMe to market carrier testing for only a single condition, Bloom syndrome. Bloom syndrome is a condition that is more common in individuals of Ashkenazi Jewish origin. In accepted clinical practice, carrier testing for this condition is only routinely offered to individuals from this specific ethnic background. The US FDA has not granted approval to 23andMe for another 110 “health-related reports” currently being marketed to Canadians.

Our concerns with DTC genetic testing services are focused on the potential for misleading and/or deceptive marketing practices, a lack of validation of test accuracy or reliability, the risk of misinterpretation of results, and their downstream implications, including issues of potential discrimination and negative effects on the Canadian healthcare system.

In our view, many DTC genetic testing providers promote the health benefits of their services while simultaneously disclaiming any diagnostic reliability. For instance, 23andMe carefully defines its service as “recreational testing” while its highly accessible and visually appealing website features prominent sections on health, inherited conditions and genetic risk factors, including a video of a woman claiming that 23andMe allowed her to be diagnosed with celiac disease. Additional stories displayed on the 23andMe website include an American family physician running a concierge practice, who raves about the benefits of this testing in improving the health of his patients. In this context, we believe a reasonable Canadian would perceive – despite the disclaimer – the services offered by 23andMe to be medical testing with important potential health care benefits.

4- http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/default.htm Accessed, April 29th, 2015
5- http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2013/ucm376296.htm
Further, while DTC genetic testing companies offer reports on inherited conditions, genetic risk factors and drug responses, the information supplied for individual conditions may be both inaccurate or incomplete, resulting in false assurance or false alarms for Canadian consumers. As an example of potential false reassurance, Geneyouin offers testing for arrhythmia. Its test includes 5 genes: four associated with Long QT syndrome (LQTS) and one associated with catecholaminergic polymorphic ventricular tachycardia (CPVT). In clinical service laboratories, testing consists of a panel of more than 4 LQTS genes and 2 CPVT genes (rather than one). A comprehensive arrhythmia panel ordered for patients through a physician (such as a geneticist or cardiologist) would also include testing for genes implicated in ARVC and often includes approximately 30 genes. Even the sensitivity of this standard clinical testing is far from perfect, so a “normal” genetic test does not exclude a potential inherited arrhythmia in a symptomatic individual. Limiting testing to fewer genes, with unregulated standards and without adequate interpretation has the potential to put Canadian patients at risk. In April 2015, Color Genomics launched sequencing of 19 genes associated with cancer. This service is available directly to consumers despite the fact that Color Genomics states that they do guarantee the analytical validity of their test.

In 2012, the Canadian College of Medical Geneticists (CCMG) published a statement on the use of DTC genetic testing. This statement made a set of recommendations, the foremost being that only scientifically valid tests should be offered. By their own admission, most DTC genetic testing services such as 23andMe have not validated their testing for analytical accuracy nor clinical validity. 23andMe explicitly states in its terms of service (Section 23. Disclaimer and Warranties) that: “(2) 23ANDME MAKES NO WARRANTY THAT [...] (c) THE RESULTS THAT MAY BE OBTAINED FROM THE USE OF THE SERVICES WILL BE ACCURATE OR RELIABLE”12. A similar disclaimer is included in the terms of services of Geneyouin: “GENEYOUIN MAKES NO WARRANTIES AS TO THE ACCURACY, QUALITY OR RELIABILITY OF OUR SITE, THE SERVICES, YOUR REPORT OR OTHER CONTENT, OR ANY RESULTS THAT MAY BE OBTAINED FROM THEIR USE.”13

Interpreting genetic data for complex traits (such as the risk of diabetes, heart disease, etc.) is extremely difficult - not only as genetic factors and environmental influences interact, but also because we, as a scientific community, do not have the

10- https://getcolor.com/#/learn/the-science Accessed April 23rd 2015
data to understand the interplay of these and other unknown factors, nor their relative weights. For example, in December 2013, an American journalist sent her DNA to 3 different companies and obtained widely divergent risk interpretations.\textsuperscript{14} Recently, the CBC program “Marketplace” demonstrated that a single consumer received dramatically different test results from 4 different DTC companies. This type of testing is misleading at best. Moreover, even for genes conferring a strong genetic predisposition, for example \textit{BRCA2}, the penetrance is rarely complete: the risk of breast cancer in a woman with a BRCA2 mutation is approximately 40-70\%, compared to 12\% for women in the general population. In other words, for every 10 women with a mutation in this gene, 3-6 of them will not develop breast cancer, a fact not well appreciated among the general population or even some healthcare professionals.

The Canada Health Care Act and our health care system aim to provide universal and fair access to health care. This implies that health care resources must be allocated equitably to those with similar needs (rather than those who pay out of pocket) and that we, as health care providers, must be responsible stewards of these resources. While one may perceive, at first blush, that consumers self-paying for a test will save the health system money, the opposite is true. A DTC test will initiate a cascade of costs as the patient, armed with raw data of unknown validity engages the health care system by seeking interpretations of the DTC results from a skilled health care provider as well as follow-up testing in clinically certified laboratories. In fact, a recent study estimated that the average cost to the healthcare system of interpretations and cascade investigations for DTC initiated testing is up to $20,000.\textsuperscript{15} We firmly believe that Canadians should decide, as a society, for which conditions and on which criteria carrier and diagnostic testing ought to be offered; once we make the decision to cover the costs, we should offer optimal testing to patients. Optimal testing includes appropriate genetic counselling and informed consent to ensure that patients are aware of the important risks, benefits and limitations of pursuing testing, as well as help and support in the interpretation of results when they become available. Genetic counselling is critical to a patient’s understanding of the potential implications of a positive result, as well as the limitations of a negative result. Genetic counselling is typically not provided in a DTC setting and, when attempted over the phone, does not include the important context provided by a patient’s medical history, physical examination findings and his/her other medical investigations.

A number of DTC genetic testing companies offer patients the option of enrolling in research, which is often a very lucrative endeavor for the company. Indeed, the

\textsuperscript{14}\url{http://www.nytimes.com/2013/12/31/science/i-had-my-dna-picture-taken-with-varying-results.html?pagewanted=all&r=0}

owner of a large repository containing both clinical information and DNA can then sell it for a profit to researchers. A substantial portion of the profit margin of some DTC genetic testing companies often derives from the profit of selling access to such databases.\textsuperscript{16} Enrollment in this research can either be provided on an opt-in\textsuperscript{17} or opt-out\textsuperscript{18} basis. An opt-in basis means that consumers must explicitly agree to contribute their sample and data to research prior to being enrolled. An opt-out basis means that consumers are automatically enrolled in research unless they explicitly withdraw. Such research does not comply with the established “Tri-Council Policy Statement on the Ethical Conduct of Research with Humans” that serves to guide the conduct of research in Canada.

Notwithstanding the unwillingness on the part of most of the DTC providers to warrant the accuracy of their tests, these results may be considered by some to represent true, clinical grade genetic test results. Thus, "direct to consumer" testing may lead to issues related to employability or insurability. In the United States, the Genetic Non-Discrimination Act (GINA)\textsuperscript{19} protects American citizens against discrimination derived from Genetic testing results. In Canada, there is currently no law to protect our population against unfair use of personal genetic information. When seen by a medical professional, patients benefit from individual and contextualized counselling regarding the risks and benefits of genetic testing prior to deciding whether or not they want to embark on such an endeavor. The question of the potential impact on future insurability is systematically discussed during such sessions. However, when a Canadian consumer opts for "direct to consumer" genetic testing, he or she may not have considered or understood the implications of the results. As such, this individual may suffer unanticipated financial, employment, emotional, and social consequences. This is all the more troubling as the unanticipated consequences stem from test results which are often not guaranteed by the provider.

Given the Federal responsibility to provide public health protection programs, we firmly believe our government has a responsibility to protect the best interests of our population by taking immediate action to ensure that Canadians benefit from reliable, accurate and medically-relevant genetic testing services. \textbf{In this context, we ask you to protect the population by recognizing health-related DTC genetic testing as a medical service and instituting a regulatory framework that will hold the providers of such testing to the appropriate professional performance standards.}

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\textsuperscript{16} \url{http://www.theverge.com/2015/1/6/7502801/23andme-60-million-genentech-funding} Accessed April 23\textsuperscript{rd}, 2015  \\
\textsuperscript{17} \url{https://www.23andme.com/en-ca/research/} Accessed April 23\textsuperscript{rd}, 2015  \\
\textsuperscript{18} \url{https://getcolor.com/#/learn/giving-back#collaborations} Accessed April 23\textsuperscript{rd}, 2015  \\
\textsuperscript{19} \url{http://www.eeoc.gov/laws/statutes/gina.cfm} Accessed April 23\textsuperscript{rd}, 2015
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Sincerely,

The Education, Ethics and Public Policy (E2P2) committee of the Canadian College of Medical Geneticists (CCMG)

Julie Richer, MD, FRCPC, FCCMG, Chair E2P2 committee

Graham Sinclair, PhD FCCMG

Alice Virani, MA (Oxon), MS, MPH, PhD

Elaine Goh, MD, FRCPC, FCCMG

Sharan Goobie, MD, FRCPC, FCCMG

Andrea Guerin, MD, FRCPC, FCCMG

Ron Agatep, PhD FCCMG

Catherine Li, PhD FCCMG

Victoria Mok Siu MD, FRCPC, FCCMG

April 20, 2015
Gail Graham, MD, FRCP, FCCMG, President of the CCMG

April 20, 2015

Cc: Prime Minister’s Office, Ministry of Justice, Ministry of Health, Senator James Cowan