The *Professional and Public Policy Committee* of the European Society of Human Genetics welcomes the work of the Human Genetics Commission in the field of direct-to-consumer genetic testing. In recent years it has read with great attention the reports *Genes Direct* and *More Genes Direct* on the actual issues of direct-to-consumer genetic testing services. In our meeting on the 30rd of November 2009 we discussed the proposed framework.

Considering the actual controversy around direct-to-consumer genetic testing, the PPPC appreciates that the Human Genetics Commission wants to set standards and principles with regard to the provision of genetic tests sold directly-to-the consumer and to promote their consistent use at an international level. The PPPC also applauds the fact the Human Genetics Commission has engaged in a discussion with representatives from companies offering direct-to-consumer (DTC) genetic testing services regarding these commercial activities.

Although we understand that the HGC draws attention to genetic issues, we would like to raise the need to broaden this discussion. The purpose of most DTC genetic testing services is to generate predictive health information. In our opinion a broader framework is needed, not only limiting the standards and principles to *genetic* information. For imaging (total body scan) and other screening possibilities similar concerns apply.

As far as in vitro diagnostics (IVDs) are concerned, we would further like to suggest that differences between the tasks of the USA FDA and EMEA need to be discussed. Standards and principles for the assessment of risks and advantages of medication, including strategies to generate knowledge in post-marketing surveillance, regulations on advertising health claims, should be similar in the IVD market. The governance of the fields of medication and IVDs needs to be closely linked. Also the possibilities and limitations of self-regulation need to be discussed.

We now come to the principles proposed. Although the Human Genetics Commission has clearly advanced that the principles have been developed with the goal of ensuring “good practice” and to safeguard the interests of the consumer (Principle 1.1.), the PPPC, nonetheless, has an important number of concerns which are not covered, or are only partially addressed by the proposed principles.

1. The Principles focus on appropriate information levels when selling genetic tests (principle 4.1.) and acknowledge that tests should “accurately describe both the characteristics and the limitations of the tests offered” (principle 2.2.) and that the “claims made about the clinical validity of genetic tests should be supported by relevant evidence published in peer reviewed scientific literature” (principle 2.3.) Although the Human Genetics Commission describes that “only clinically validated genetic variants should be used”, it is clear that most of the variants currently used by most of the companies do not meet the standards for clinical use. As Janssens et al. (2008) [1] advanced, “there is insufficient evidence to conclude that genomic profiles are useful in measuring genetic risk for common diseases or in developing personalized diet and lifestyle recommendations for disease prevention.” A list of guiding principles, although a welcome step in promoting higher standards, can not properly address the offering of direct-to-consumer genetic tests which are nearly all, to varying degrees, inaccurate, misleading or simply useless. According to the PPPC, the current guiding principles focus too much on the requirements the test providers should fulfill while paying too little attention to the ***quality*** of the genetic tests that are being sold. The PPPC remains concerned about the quality of the tests provided and believes that the clinical validity (and not only the analytical validity) of genetic tests should be proven before one can even begin to consider selling such tests directly to consumers.

2. Although the Principles describe many requirements for providers in order to ensure that they "supply easily understood, accurate, appropriate and adequate information to consumers before obtaining consent" (principle 4.1.), the PPPC considers that the responsibility towards test providers is exclusively placed on the supply of information to prospective consumers. Although the provision of this information is essential, the PPPC considers that the Principles reduce the informed consent process to a process in which the test providers have to provide sufficient and appropriate information and "should require consumers to sign a statement confirming that they give informed consent to the specific genetic tests to be undertaken on their biological material" (principle 5.4.). In this way, informed consent has become synonymous with the "consent form", a legal invention with a legitimate role in documenting that informed consent has taken place, but hardly a substitute for the discussion process leading to adequate informed consent. Informed decision making is a process, not a signature of click of the mouse. Although test providers might say that all information (and limitations) about the sold genetic tests are available on their website, the PPPC considers that the current Principles do not put enough responsibility on the test providers to ensure that the consumers comprehend the disclosed information, act voluntarily, and are competent to act and consents to all elements of the consent form. Providing information does not substitute obtaining informed consent. Moreover, who decides what is "accurate and appropriate information?" This is particularly disturbing, because a great portion of the concern with regard to direct-to-consumer genetic testing lies in particular in the misunderstanding of the genetic information by potential users. For example, the results from McGuire[2] et al.'s study (2009) suggest that a portion of social networkers who responded to their survey believe that personal genome testing (PGT) offers medically relevant and potentially important information, even diagnostic information. They report that 34% (374/1087) of all survey respondents (including a majority who have not used PGT) believe the information provided by PGT to be a medical diagnosis. Moreover, of those who *have* used PGT, 60% (38/60) consider the information obtained from PGT to be a diagnosis of medical condition or disease. This is of particular interest for many reasons, one of which being that many companies, including those mentioned in McGuire et al.'s survey (2009) in fact, have statements/disclaimers on their websites stating that their services are not meant to have a formal medical purpose.
Tests should be stratified to genetic tests with the potential to identify a high risk of a serious disorder vs. other tests. The former type of tests should not be available without a face-to-face genetic counseling session by a medical expert such as a clinical geneticist or genetic counselor. Furthermore, they should not be included in a "package" including tests for different purposes.

3. Although Principle 9.1. underlines that "there should be no remuneration structure in place that would allow this individual to benefit directly from any particular interpretation of the test results or the sale of any services or products related to those results", the PPPC has concerns about the attainability of this principle and worries about the impartiality of genetic counselors hired by these test providers. If a company's profits are dependent on selling tests, then how could employees hired by that same company or representing that company be completely impartial and not (routinely) suggest testing to potential clients?

4. Based on the principles of respect for autonomy, confidentiality and privacy, and the potential psycho-social impact of genetic information on children and their family, the PPPC supports the Principle 5.10 to postpone genetic testing of children until that child has the capacity to consent. The PPPC does support the view that in a clinical context the opinion of a minor should be taken into consideration as an increasingly important determining factor in proportion to his age and degree of maturity. In the specific context of a provision of genetic tests sold direct-to-consumer, however, it is impossible to assess the competence of a minor. The PPPC therefore advices that Principle 5.10 should state that genetic tests directly-to-consumers should not be available to individuals who have not reached the age of legal majority.

5. The PPPC raises additional concerns regarding the fact that that the provision of genetic tests outside the health care system may consequently lead consumers to visit health care professionals (as a follow up to the genetic test results) and result in an overconsumption of health care services. Principle 4.10 also recommends that "where appropriate, the test provider should supply consumers with information about genetics health professionals who are able to offer further advice or support." This is particularly worrisome given the fact that test providers may sell genetic tests directly-to-consumers which do not meet criteria for use in clinical practice, but are sending consumers to the healthcare system for advice or support. The PPPC considers this an inadequate practice. Possible consumer confusion regarding the medical value or interpretation of results is but one concern regarding DTC genetic testing which is highlighted in the report by McGuire et al. (2009) The fact

that 78% of those who would use PGT services, would also then ask help to interpret results from a physician could also be indicative of the possibility of needless visits to the physician's office and use of medical services. Principle 4.10 is in fact unwillingly supporting the potential overconsumption of the healthcare system and this is particularly worrisome in a publicly funded healthcare system.

6. Regarding genetic tests in the context of inherited or heritable disorders (i.e. diagnostic tests, pre-symptomatic genetics, carrier tests), the Human Genetic Commissions recommends as a principle that these tests should only be provided to consumers with individualized pre-and post-test counseling. The PPPC believes in a more restrictive position and considers that it is entirely inappropriate to offer this type of genetic tests directly to consumers in the case of a potentially high risk of a serious disorder. There is an established professional policy of traditional clinic-based genetic counseling delivered by trained genetic counselors and clinical geneticists, that has been built after decades of input from patient organisations and medical professionals. There is hardly any evidence whether telephonic individual pre-and post-test counseling might be an appropriate substitute for face-to-face contacts with patients in a genetic setting. Providing principles in which individual pre and post-test counseling are recommended as necessary conditions for these types of disorders, seems to acknowledge that direct-to-consumer genetic is an appropriate alternative for traditional clinic-based testing and genetic counseling. We do not support this statement.

7. Principle 5.3. highlights that test providers should "take reasonable steps to assure themselves that a biological specimen provided for testing is obtained from the person identified as the sample provider". The PPPC does not see how in a model of direct-to-consumer provision of genetic tests this can ever be truly achieved.

8. When discussing ethical, legal and social issues of direct-to-consumer genetic testing many different fields of study contribute to the debate. As such, language and definitions should be as precise and clear as is possible and should be consistent for geneticists, clinicians, social scientists and members of other disciplines taking part in the debate. As definitions might have important implications, we ask to reconsider following notions.

- Vague terms such as "phenotype tests" and "genetic matches" should be avoided. All genetic tests are ultimately a phenotype tests, and this is not a term commonly used in genetics. Based on the definition given, it seems to mean "non-disease-related-traits" As for the latter, is it meant in the context of ancestry or in the context of romantic match-making (i.e.: http://www.scientificmatch.com/html/index.php)?
- The term "Genetic health professional" is too broad as defined here. What is "appropriate" training and what are the "required competencies" and who or which guidelines define these? We refer to guidelines published by EUROGENTEST.
- "Genetic test in the context of inherited or heritable disorders" include the first three categories of tests (diagnostic tests, presymptomatic tests, carrier testing) and deliberately exclude for example pharmacogenetic tests and susceptibility/predispositional tests. However, taking into consideration many claims of DTC companies all these tests are "capable of providing information that may have important implications for the health of the person…" It is therefore, questionable why some tests might require pre-and post-test genetic counseling and others not. We refer to the report on the definition of "genetic testing" published by EUROGENTEST.
- Currently, the principles don't cover genome testing in which companies are testing thousands of SNPs (e.g. 23andme, Decodeme, Geneessence, Navigenics) or performing whole genome sequencing. The PPPC has concerns especially when offers for recreational purposes are mixed with tests for a potentially high risk of serious disorders as well as susceptibility to common disorders.

Reference List

(1) Janssens AC, Gwinn M, Bradley LA, Oostra BA, van Duijn CM, Khoury MJ. A critical appraisal of the scientific basis of commercial genomic profiles used to assess health risks and personalize health interventions. Am J Hum Genet 2008 Mar;82(3):593-9.

(2) McGuire A, Diaz CM, Wang T, Hilsenbeck S. Social Networkers' Attitudes Toward Direct-to-Consumer Personal Genome Testing. Am J Bioethics 2009.