

# Direct-to-consumer genetic testing: from ethical concerns to policy answers

Pascal Borry<sup>a</sup>

<sup>a</sup> Department of Public Health and Primary Care, KU Leuven, Belgium

The offer of genetic testing has traditionally been embedded in a clinical setting, where patients and their relatives can get access to diagnostic or predictive genetic tests which have impact on their health and reproductive choices. The provision of these genetic testing services happens in a context where an emphasis is placed on individualized medical supervision, pre-test and/or post-test counselling, and psychological support. In recent years, various companies have been offering genetic tests outside this usual setting. As *Nature* portrayed it a few years ago: «the availability of affordable, direct-to-consumer genetic tests has mushroomed.» [1]

Direct-to-consumer (DTC) genetic testing can be defined as the advertising, selling or (free) provision of genetic tests directly to consumers. As suggested by a report of the Human Genetics Commission, this also includes «tests that are commissioned by the consumer» but where a health professional is involved in the prescription of the test or in the interpretation of the test results [2]. The general process through which a genetic test can be ordered is similar for all companies: a test kit is ordered online (with or without a medical prescription), a test tube is sent to the consumer's home and must be filled with saliva, the company extracts the DNA and then analyzes the DNA, and finally the company provides the results on a password-protected website. The type of tests that are currently being sold by DTC companies (primarily through the internet) include carrier tests for autosomal recessive or X-linked disorders, risk profiles for common complex disorders or traits, pharmacogenomic tests, paternity tests, non-invasive gender determination tests, and ancestry or genealogical tests. Despite the variety of tests on offer, most companies usually refer to the right of individuals to access their genetic information, the possibility to adapt their lifestyle or make health-related decisions based on the information, the empowering character, and the fact that only the test applicants will receive the test information (and not health care professionals, insurers or employers) [3].

The phenomenon of DTC testing has led to a number of policy reports and statements. Various professional groups and genetic societies have discussed the topic [4–8]. In addition, numerous National Bioethics Committees [9–12] and national advisory committees [2;13] have also addressed the subject. Most recently, the European Academies of Science and the Federation of

European Academies of Medicine have published a report on the subject [14].

Various concerns have been raised in relation to DTC genetic tests. A major issue is related to the limited value of risk prediction models for common complex disorders which are based on low risk variants. As described by Janssens et al. [15], «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». Multifactorial disorders are hypothesized to occur due to a complex interaction of multiple genes and environmental factors. Each genetic and environmental factor often contributes only a modest fraction of the risk of developing the disorder, therefore, making it extremely difficult to assign an accurate and meaningful degree of risk to each different factor. This concern also applies in the context of carrier identification of autosomal recessive disorders, where interpretation of certain mutations might be unclear because expression might be variable [16].

Furthermore, a potential consequence of the provision of DTC genetic testing services is a downstream impact on the healthcare system. Various studies have shown that some consumers are looking for counselling and medical follow-up after having bought such a test [17–20]. Most DTC genetic testing companies also refer consumers to the regular healthcare system for interpretation of their test results. This issue may become even more problematic in the future if the upcoming trend of companies offering whole genome sequencing DTC without interpretation of the sequence results continues to grow.

Other concerns are focused around the provision of information to consumers, the absence of genetic counselling and the lack of an adequate informed consent process. Examples have been provided of companies overstating the potential predictive value of their tests and their future health implications [21]. The absence of genetic counselling accompanying the provision of test results might also impact the interpretation of test results. Consumers who obtain a test revealing a form of increased risk may over-estimate the risk they have of developing the disease; consumers obtaining a decreased risk may under-estimate the risk of still developing that disease. Furthermore, the process of obtention of DNA samples involved in DTC genetic testing does not allow for a control over the origin of the

samples being analyzed. Since the samples are collected at home, there is no way of controlling for the identity of the sample provider. This might allow individuals to analyze the DNA of third persons without their consent [22]. Finally, concerns have also been raised with regard to the fact that DTC genetic testing companies process samples from minors [23–25] and the fact that DTC companies use consumer data for research activities [26; 27].

In response to the development of DTC genetic testing services, various policy actions and initiatives have been elaborated, and various other suggestions for actions have been provided. These include initiatives for education of the general public and healthcare professionals about the limitations and concerns regarding DTC genetic tests [28–30]. An initiative was also elaborated by the Human Genetics Commission with the aim to guide self-regulation by commercial testing services [2]. France has now prohibited individuals from ordering DTC genetic tests, with a potential fine if individuals order them [31]. Suggestions were also provided to introduce a quality mark or label (such as an ISO norm) for DTC genetic tests in order to ensure that the product provided is compliant with ethical standards, has scientific validity and includes counselling and/or medical supervision [32].

Already, before the advent of DTC genetic testing, one of the most common approaches to regulating the provision of genetic testing for health purposes has been to make genetic tests available only through medical prescriptions along with the inclusion of counselling and appropriate informed consent. Various European countries have enacted such legislation in recent years [33]. The German law (Genetic Diagnosis Act, GenDG) [34] describes that a diagnostic genetic examination may only be performed by a physician and that a predictive genetic test can only be undertaken by a medical specialist in the field of human genetics. Moreover, genetic tests can only be provided after sufficient information concerning the nature, meaning and consequences of the genetic test and after the consent of the person concerned. The French law also integrates the provision of genetic tests in a medical relationship, integrating specific requirements with regard to the information provision, the consent, and the counselling. In Portugal, the Law n° 12/2005 of 26 January 2005 [35] defines that most genetic tests can only be carried out after the request of a medical geneticist, following a genetic counselling session and subject to the informed consent of the person in question (which should be written).

These national legislations mirror some of the recommendations that have been integrated within the additional protocol to the Convention on Human Rights and Biomedicine concerning genetic testing for health purposes [36]. This document states that «a genetic test for health purposes may only be performed under individualised medical supervision». As we can read in the explanatory report, this article has been «driven by the

concern to enable the person concerned to have suitable preliminary information with a view to an informed decision regarding the carrying out of this test and, if appropriate, to have access to an appropriate genetic counselling. A precise evaluation of the situation of the person concerned, involving direct contact with him or her, is a determining element in that respect. A mere telephone conversation with a medical doctor, for example, does not allow for such evaluation.» [37] This additional protocol emphasizes, among other issues, the importance of genetic counselling, free and informed consent, the protection of persons not able to consent, the respect for private life and the right to information.

The purpose of these legislations is clearly to embed genetic testing in a healthcare setting. It is based on the notion that this setting is the most appropriate to provide genetic tests. It assumes that the absence of medical supervision for most genetic tests may compromise or fail to foster patient health. It advances that in the healthcare system most individuals will have access to the tests they really need and under conditions in which they receive adequate information, the appropriate counselling and follow-up, and the necessary psychological support if necessary.

Recently some companies have changed their policies and practices about the way DTC genetic tests can be ordered. Various companies now ask a medical prescription before a test can be processed and test results are often also shared with the ordering physician. This has raised questions about the potential conflict of interests if physicians that are involved in the counselling are employed by or linked to the companies selling the tests. In this case impartial health advice might be compromised [38].

The offer through physicians may eliminate some of the concerns that have been raised about information provision, but does not address the issue about the appropriateness of the test provided. As described earlier, one of the main problems with many of the tests currently on the market is their (lack of) clinical utility. Advocates of DTC genetic testing companies have advanced that the tests that are being sold might have personal utility [39]. This interpretation of utility is at odds with attempts from the professional community of clinical geneticists to develop common standards of clinical utility. Examples of such initiatives include those being developed by the UK Genetic Testing Network,<sup>1</sup> the EU-funded Eurogentest network of excellence<sup>2</sup> and the Evaluation of Genomic Applications in Practice and Prevention.<sup>3</sup>

At the European level, the market authorization of genetic tests falls under the scope of the Directive

1 Gene Dossiers, <http://www.ukgt.nhs.uk/gtn/Information/Services/Gene+Dossiers>

2 Gene Cards, <http://www.eurogentest.org/web/info/public/unit3/geneCards.xhtml>

3 EGAPP, <http://www.egappreviews.org/>

98/79/EC on in vitro diagnostic medical devices. This Directive, adopted in 1998, aimed to create an internal market for IVD medical devices and to ensure that such devices meet essential requirements regarding their safety and performance when placed on the market in the European Union. In September 2012, the European Commission presented a proposal for a new legal instrument after several years of public consultations. Instead of a Directive, this instrument would be a Regulation which means that this piece of legislation will be immediately binding for all Member states without a transposition into national law being necessary (European Union). This proposed regulation is still under discussion at the European Parliament and will be presented for a vote in September 2013. Although a new risk classification has been proposed, which would lead to the requirement of premarket approval for all genetic tests for health purposes, it is clear that the notion of clinical utility was not integrated in the proposed Regulation. This issue was raised by some of the voices during the public consultation, which support the notion that clinical utility should not constitute a part of the pre-market assessment process. This is because clinical utility is considered to be a «moving concept» that could be more effectively regulated on the Member State level [40]. It was also suggested that «clinical utility should not be demonstrated by the manufacturer, but should be assessed by the user. The user would have to decide on the clinical utility of a specific IVD medical device in a specific context or a specific population.» Furthermore, it was reported that, in many cases, it would be impossible to demonstrate the clinical utility and that this would «limit the market access for innovative IVD medical devices» [40].

The main problem with this approach is that there is currently «no requirement that approval of high and medium risk devices should be based on high quality evidence of benefits that are relevant to patients» [41]. Efforts in the assessment of tests are also necessary at an international level, and not only at a national level. However, we might learn from initiatives realized at a national level. It might be useful, for example, to reflect on the advantages and disadvantages of legislation such as the Dutch Act on Population Screening, which aims to supervise tests that are offered to the entire population (or a part of it) by a permit system [43].

In conclusion, a greater focus should be placed on the clinical utility of genetic tests. Although the definition of clinical utility may differ among stakeholders [43], it is important to address the topic and make sustained efforts in order to ensure that clinically useful tests are promoted and less useful tests are discouraged. This goal should not only be achieved in relation to DTC genetic testing, but more generally for every genetic test being performed in the health care or public health settings. In order to achieve this goal, the development of assessment procedures addressing the usefulness of genetic tests will be necessary.

## Correspondence

Prof. Dr. Pascal Borry  
Interfaculty Centre for Biomedical Ethics and Law  
Department of Public Health and Primary Care  
Kapucijnenvoer 35 blok d - box 7001  
3000 Leuven

E-Mail: pascal.borry[at]med.kuleuven.be

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