Predicting the future of EU genetic testing regulation – opportunities and pitfalls

How should genetic tests be regulated in the EU? What special provisions should there be given the potential far-reaching impact of a patient learning they have an incurable disease, for example? Should they be freely available on the Internet, and how can users be protected from advertising? Joanna Hook and Grant Strachan, associates in the regulatory department of law firm Bristows LLP, look at the current regulation of these tests and at how the EU is likely to become much more challenging for manufacturers with the future revision of its IVD requirements.

Genetic testing provides great potential for enhanced knowledge about our genetic make-up which in turn informs us of our potential predisposition to certain inherited conditions. Whether an individual wishes to find out about their predispositions is another question.

Until recently, genetic testing was limited to specialist medical genetic services which provided patient information on rare inherited genetic disorders. However, the rapid pace of scientific advancement in gene sequencing has made DNA analysis cheaper and faster. This development has sparked an increased interest in the development of genetic tests for determining susceptibility to a broader range of disorders. These tests are also increasingly being offered direct to consumers (DTC), including via the Internet, without necessarily involving health care professionals.

According to a recent forecast by Global Industry Analysts, the global DTC genetic testing market is projected to reach more than $233m by 2018. However, as a rapidly evolving area within the laboratory testing industry, DTC genetic testing has generated considerable scrutiny from governments, scientists and consumers alike.

This article focuses on the current EU regulation of genetic tests and how future legislative changes will likely shape the regulatory framework in this groundbreaking field of scientific and medical innovation.

**Concept of DTC genetic tests**

In the context of DTC genetic testing, consumers looking to obtain information about their genetic health are usually asked to collect their own sample for analysis. This normally takes the form of a small quantity of saliva or a cheek swab. This sample is then posted back to the supplier’s laboratory where the subject’s DNA is extracted and analysed. Often, the subject can access the results via the Internet through a password-protected website. Consequently, geographic location is no longer a restriction on the ability to obtain genetic testing services. DTC genetic testing represents a paradigm shift in control from the clinical domain and medical professionals into the hands of consumers. However, such a shift has profound ethical and legal implications.

**Current EU regulation**

Although not specifically mentioned per se in the In Vitro Diagnostic Medical Devices Directive 98/79/EC (IVD Directive), genetic testing kits come within the definition of an in vitro diagnostic medical device (IVD) and must bear the CE mark. With the IVD Directive dating back to 1998, the pace of scientific advancement is moving faster than the legislation in this area and so advising on these issues can be challenging.

As well as the IVD Directive, national laws and EU and national guidance apply. EU level guidelines and international standards, including those developed by the Organisation for Economic Cooperation and Development (OECD), the Council of European Union and professional bodies like the European Society of Human Genetics, serve to provide enhanced and complementary guidance.

The IVD Directive regulates IVDs that are intended to examine human specimens for a medical purpose, such as providing information about a physiological or pathological state or concerning a congenital abnormality (for example, a genetic test for evaluating the risk of Trisomy 21 in pregnant women). ‘Specimen receptacles’ are also considered to be IVDs if they are intended for the primary containment and preservation of human specimens for in vitro examination, and so they must bear the CE mark. Even if the receptacle is not used as part of the analysis, the fact that the human specimen is collected and transported in that receptacle would form part of the process leading to the analysis, and so the receptacle would fall within the scope of the IVD Directive.

There is an ‘in house’ exemption...
from the requirement to CE mark a product under the IVD Directive but this is very limited in scope. Broadly speaking, it applies when the device is manufactured and used only within the same ‘health institution’ and on the premises of its manufacture or in the immediate vicinity. In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) considers a ‘health institution’ to be a body whose primary purpose is the care and/or promotion of public health, like NHS trusts and bodies such as the National Blood Authority and the Health Protection Agency. The exemption would not apply, for example, to genetic tests offered by private companies specifically targeting UK consumers for commercial exploitation.

It is the company that places the testing kit on the market that is treated as the “manufacturer” for purposes of compliance with the IVD Directive, irrespective of whether the operations of design, manufacture, packaging and labelling are carried out by that company or by a third party. It is also not necessary for a company to have a physical presence in the EU in order to be subject to the legislative requirements. If a company places an IVD on the EU market, but it does not have a registered place of business in one of the countries of the European Economic Area (EEA), Switzerland or Turkey, it must appoint an “authorised representative” in order to comply with the IVD Directive.

One advantage of qualification as an IVD is that once the testing kit is CE marked in accordance with the IVD Directive, it can be placed on the market and circulate freely within the EEA, Switzerland and Turkey. This currently gives access to over 30 countries.

**Advertising restrictions**

Companies marketing diagnostic screening tests should be very careful with advertising claims to ensure they comply with the applicable rules in the country where consumers will be targeted. Even if the website advertising the DTC genetic test includes some form of disclaimer, a regulator is likely to regard the provision of the information directly to consumers as de facto provision of medical information (if there is some form of diagnostic service), and so will treat the testing kit as an IVD.

There are currently no general restrictions under EU legislation on the marketing of CE marked IVDs directly to consumers, although this is likely to change in the future. We discuss this issue further below. However, specific sectoral legislation in the UK (for example) does prohibit, amongst others, the advertising and promotion of HIV testing kits to the UK public. Under other UK legislation, advertising which may lead to the use of ‘substances or articles’ (which could therefore catch IVD testing kits) for the diagnosis or treatment of certain specified diseases, like cancer and diabetes, is also prohibited unless under the instruction of a doctor.

**Human tissue requirements**

As well as the IVD Directive, companies need to consider national legislation regulating activities concerning the removal, storage, use and disposal of human tissue to ensure they are fully compliant.

For example, the Human Tissue Act 2004 (HT Act) (which applies to England, Wales and Northern Ireland), regulates the removal, storage and use of human tissue. This is defined as material that has come from a human body and consists of, or includes, human cells. Consent is the fundamental principle of this legislation. The HT Act also imposes licensing requirements on companies depending on the primary purpose for which a sample is taken and stored. If the primary purpose for taking the sample is for a diagnosis, then storage of that tissue is not licensable under the HT Act. However, if a broader use (like research) is intended, a licence will be required.

**Classification**

The EP’s proposed amendments text defines a ‘device for genetic testing’ as an IVD the purpose of which is to identify a genetic characteristic of a person which is inherited or acquired through prenatal development. Devices for genetic testing are classified as Class C in the Commission’s IVD Regulation (and accepted as such in the EP’s text) which means they are amongst the higher risk devices and can only be supplied on a medical prescription.

**Ban on DTC advertising**

A key article in the text of the amendments agreed by the EP places a ban on DTC advertising of devices for genetic testing. A device may only be used for the purposes of a genetic test if the indication is given by a person admitted to the medical profession after a personal consultation. This is a material development and would serve to seriously constrict market access for the majority of genetic testing companies who currently offer some form of DTC service. Notably, this proposed prohibition on DTC advertising of prescription IVDs effectively mirrors the strict
requirements in the EU pharmaceutical legislation.

If this proposed amendment is carried through into the legislative text, it would mean that companies would have to re-evaluate their commercial approach because they would no longer be able to legally target EU consumers by advertising and selling genetic screening tests directly to them. As a result, the only viable alternative would be to introduce the products to healthcare professionals to provide to patients on prescription and this would dramatically impact the product marketing and pricing strategy.

**Genetic counselling and informed consent**

The European Parliament has also introduced strict rules around genetic counselling and informed consent into the draft IVD Regulation which will serve to protect patients and ensure that any tests are carried out in an ethical manner with the appropriate amount of support for the individual. The proposals expressly provide that a genetic test must protect the rights, safety and well-being of the test subject and clinical data generated in the course of the genetic testing must be reliable and robust. Explicit reference is also made to the principles set out in the European Convention on Human Rights and Biomedicine, and the Additional Protocol to that Convention concerning Genetic Testing for Health Purposes.

**Stricter pre-market requirements**

Given the Commission proposal, and further amendments added by the EP, it looks likely that stricter pre-market obligations will be imposed on IVD manufacturers. For example, according to the EP text, a manufacturer is required to draw up a report on the safety and clinical performance of the device based on the full information collected during the clinical performance study. This report would then be part of the documentation to be submitted to and validated by the notified body. The EP has even proposed that a summary of the technical documentation should be made publicly available. By way of post-marketing surveillance measures, the proposed amendments would require the Commission and the Member States to take “all appropriate measures to ensure the establishment of registers for in vitro diagnostic devices to gather post-market experience related to the use of such devices.”

Whilst a number of changes have been introduced to strengthen the regulation of genetic tests, some commentators argue that the Commission’s proposal for an IVD Regulation does not go far enough. For example, there is (i) no pre-market review or publication of the manufacturer’s data on clinical validity; and (ii) no requirement to provide, review or publish data on clinical utility. The EP, however, does pick up on the issue of clinical validity and clinical utility and would like to see evidence of both of these factors, including making them available to users.

We will have to wait and see how the legislation develops. Even if the text is agreed before May 2014 when the European elections will be held, the IVD Regulation would not likely apply until 2017 at the earliest.

**Conclusion**

In a rapidly developing field, genetic testing is likely to see many new developments and changes in the near future. These types of services undoubtedly offer tremendous potential and advances in genetic innovation promising healthcare as well as wider societal benefits. However, despite the tangible prospects, this is a market fraught with challenges. There are a variety of social, ethical, clinical and legal issues that have yet to be considered in-depth.

Significant concerns have been expressed about the quality and validity of some of the genetic tests offered, the clinical usefulness of the information supplied and the implications for patients, their families and the public health services.

From a regulatory perspective, adopting an EU regulation with rules on genetic testing is crucial to ensure harmonization throughout Member States. The legislation that is implemented must realize the importance of protecting individuals’ rights whilst simultaneously setting appropriate standards that permit effective market exposure for companies providing accurate and reliable services in this exciting and evolving sector.

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