ITALIAN JOURNAL OF PUBLIC HEALTH

Quality assurance in genetic testing: a European perspective

Dolores Ibarreta[1], Line Matthiessen-Guyader[2]

[1]DG Joint Research Centre (JRC-IPTS), European Commission; [2]DG Research, European Commission

Correspondence to: Dolores Ibarreta, European Commission, Joint Research Centre, IPTS Institute for Prospective Technological Studies, Edificio Expo C/ Inca Garcilaso, s/n, E-41092 Sevilla, SPAIN. Email: dolores.ibarreta@ec.europa.eu

Abstract

Genetic testing has moved rapidly from research to clinical use and the issues of quality have not always received sufficient attention. In response to these needs to improve the overall quality assurance system for genetic testing and services there have been several international initiatives that are reviewed here. The main activities at European level towards improving the quality assurance of genetic testing are described.

Key words: genetic testing, quality assessment, reference systems, international cooperation

Introduction

Genetic testing is a relevant example of leading-edge research and development - showing potential for the benefit of society - and at the same time having important policy implications for research, public health, regulation, fundamental rights, ethics and international cooperation.

Testing for genetic diseases has rapidly moved from the laboratory into medical use and, in the process, issues of quality have not always been given sufficient attention. Genetic services in Europe, while based on high quality scientific know-how, are not free from technical errors and quality issues in determination and reporting. At the same time there is a clear European dimension in terms of marketing and use of genetic testing across borders. Although genetic specialists and professional organisations have initiated moves to promote quality assessment, genetic testing services are provided under widely varying conditions, diverse and heterogeneous quality schemes, lack of reference measurement systems and differing Member State (MS) regulations. These issues have also been addressed at international level and the OECD recommended in a report from 2001 [1] that a comparative analysis of emerging patterns in the organisation of genetic services and quality assurance systems across OECD countries should be conducted to facilitate an understanding of the factors influencing the availability of tests and services and the policies to be developed to meet the expected increase in demand [2,3].

The lack of an adequate quality assurance system for genetic testing has in the short term important consequences for the person tested and his/her family and in the long term it may increase public mistrust in biotechnology and in the capacity of public authorities to ensure proper governance of biotechnology. According to the Eurobarometer 2005 [4], 58% of the responders support the use of personal genetic data. A continued support will depend on the capacity of public authorities to ensure proper governance of the use of genetic information. Action at EU level for improvement concerning organisation and defragmentation has already started.

European activities towards improving the quality of genetic testing

In 2000, a Temporary Committee of the European Parliament focussed on the implications of human genetics and other advanced medical technologies was established. The final report of this Committee noted that genetic testing fell outside current European regulation, that there were no common European rules to guarantee service standards and that there was a need to address this issue [5]. The report also recommended the establishment of a European Network to ensure the public's access to genetic testing services for rare genetic conditions. It was also recognised that there is an increasing trend for samples for genetic tests to cross international boundaries and that this highlighted the need for an international approach to harmonising Quality Assurance (QA).

Finally, the European Parliament (EP) in the report on the Commission communication from October 2002 on Life sciences and biotechnology- a strategy for Europe called "*on the Commission to draft a legislative regulation for the introduction of a standard for genetic tests, since these services lie outside the scope of Council Regulation (EEC) N° 2309/93 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary*

use and Directive 98/79/EC on in-vitro diagnostic medical devices, which applies only to products to be marketed" [6].

The Institute for Prospective Technological Studies (IPTS) of the European Commission's Directorate General Joint Research Centre (JRC) completed a first survey to assess the situation of provision of genetic testing in the EU [7].The study identified shortcomings and measures to ensure the highest quality of such services, including:

- harmonised quality control of genetic tests and the counselling that accompanies them,
- development of a common range of certified reference materials,
- better cross-border co-operation including the establishment of a network for genetic testing of rare diseases, and the establishment of a European database of genetic testing centres

The establishment of a European/international network of reference centres seemed required [8]. In summary, a European, or even higher international level, approach was then suggested. Networking and integration at the different levels in the process of genetic testing was required to fill the gaps identified in the area.This networking was proposed as a European "*network of networks*", a virtual body or infrastructure for harmonization of practices in genetic testing.

In February 2003 in a statement, the European Group on Ethics in Science and New Technologies (EGE), an independent, pluralist and multidisciplinary body which advises the Commission on ethical aspects of science and new technologies warned against the risks of advertising genetic testing via the Internet [9] in particular due to the serious concerns raised from the perspective of fundamental rights and the private life of the person. The Group also addressed the ethical and legal issues of genetic testing in the workplace and adopted an Opinion on this subject on 28 July, 2003 (Opinion nr 18 on "*the ethical aspects of genetic testing in the workplace*") [10].

The ETAN-STRATA high level group composed of representatives from pharmaceutical companies, NGOs, patients organisations, scientists and ethicists and legal experts set up by DG Research in 2003 called for actions at EU level and gave 25 recommendations [11]. These recommendations were also discussed in a public conference organised in Brussels on May 6-7, 2004 ("Human genetic testing, what implications?") [12].

The need for further actions at the European level was recognised by the European Commission and it proposed in the second and third progress reports, on the implementation of the Life Sciences and Biotechnology strategy [13], a number of actions to be undertaken.

In the 2004 second progress report, the Commission proposed the following actions:

- to engage in EU-wide co-ordination of efforts to ensure the highest quality of genetic testing in the EU and beyond EU-25,
- to establish EU-wide networking of national centres for exchanges of information regarding quality assurance of genetic testing, including training activities, and EU-wide networking for genetic testing of rare diseases.

This was complemented in the 2005 third progress report, by a call for action to:

- enhance an EU-wide exchange of information on best practice and cooperation on the development and use of genetic testing through the open method of coordination. In particular, an evaluation of the clinical validity/utility of genetic tests and the establishment of a referral system at EU level for genetic testing of rare and complex diseases will be addressed in 2005- 2006;
- take whatever action appropriate or required, as arising from the coordination;
- launch an initiative on the protection of workers' personal data in the employment context, taking account of the European Group on Ethics in Science and New Technologies Opinion No 18 "Ethical Aspects of Genetic Testing in the Workplace".The initiative will also address the processing of genetic data;
- analyse the possibility of setting standards on genetic testing under Article 152 or 153 of the Treaty and the appropriate legal instrument;
- analyse the Directive 98/79/EC on in vitro diagnostic medical devices in the context of genetic testing and in particular regarding quality and performance assurance of genetic test devices;
- launch a mapping and networking exercise on public health aspects of genetic testing.

In order to enhance an EU-wide exchange of information on best practice and cooperation on the development and use of genetic testing the Commission established an informal network on genetic testing with experts and officials from EU Member States in 2004. The network meets each year to exchange information about national activities and discuss the way forward to ensure the highest quality of genetic testing in the EU. Based on the work of the informal network a survey on national legislation and activities regarding genetic testing was prepared in 2005 and is now being updated [14].

The Commission in collaboration with Member States has actively contributed to the drafting of the

Organisation for Economic Co-operation and Development (OECD) Guidelines for Quality Assurance in Molecular Genetic Testing, which have recently been put for public consultation [15].

A European initiative "EUHEALTHGEN" has been launched in 2004 to promote the translation of the outputs from research on population genetics into direct health benefits for European citizens. It is jointly funded by the Health Research Directorate, DG Research, European Commission, and the Wellcome Trust.

A research project, EuroGentest [16], funded under the 6th Framework Programme for Research, was launched in 2005 with the aim to develop the necessary infrastructure, tools, resources, guidelines and procedures that will structure, harmonize and improve the overall quality of EU genetic services. This Network addresses the above-mentioned needs by involving leading experts from across Europe and elsewhere. It is also believed that EuroGentest has wider implications for European healthcare. An estimated 30 million people now suffer from a genetic disease within the enlarged community. Both new and existing member states find genetics causing an increasing burden upon their healthcare systems, by the latest estimates 500 million euros [8]. Through EuroGentest, a framework for finding cost-effective solutions could be potentially supported [17, 18].

Finally, in January 2006, the Public Health Genomics European Network [19] (PHGEN) was launched, funded by the EC under the EU Public Health Programme [20]. This Network is described elsewhere in this issue.

Conclusions

Genetic testing and its scientific, ethical, legal and social implications are being debated both nationally and internationally. Discussions on the need for new legislation or, in some cases, a review of existing legislation have been initiated across Europe and draft guidelines for Quality Assurance in Molecular Genetic Testing, as already mentioned, are being prepared by OECD. Many activities at European level addressing genetic testing and in particular regarding its quality and performance assurance are taking place. The European Commission is conscious of the far-reaching consequences that the lack of an adequate quality assurance system for genetic testing might have for the person tested and his/her family. Without wishing in any way to interfere with Member States' competence regarding genetic testing, the European Commission intends to continue to contribute to a coordinated and coherent framework for the use of genetic testing in the EU.

For the immediate future, while the many ongoing activities already mentioned are effectively increasing the overall quality, there are still gaps to tackle. The increasing trend to expand from monogenic testing to a wider scope of susceptibility testing is putting pressure on the clinical system as validation of the markers and the establishment of the clinical utility of this type of tests is not developing at the same speed. Some of the activities of the above-mentioned network EuroGentest are focusing on guidelines to establish the clinical validity and utility of the tests while PHGEN is trying to incorporate health technology assessment approaches to genetic testing. OECD has also embarked in the potential needs of clinical validity assessment.The expected clinical uptake of pharmacogenetics will add up to the needs in test validation. In a society with an increasing economic burden from health care expenses, clear clinical utility of these genetic tests and the assessment of their cost-effectiveness become more important as their use becomes more widespread.

The potential ethical and societal consequences of the expansion of genetic tests from mendelian monogenic disease to more complex disease and susceptibility markers, pharmacogenetics, nutrigenetics and other ramifications, as well as the growing use in preimplantation genetic diagnosis should not be overlooked. Some of these issues do go beyond the quality of these tests but all of them would arguably fall within a proper system of quality genetic testing services.

Disclaimer

This publication expresses the views of the authors and should not be regarded as a statement of the official position of the European Commission.

References

1) Genetic Testing Policy Issues for the New Millennium. Available at: http://www.oecd.org/document/16/0,2340,en_2649_34537_1895632_1_1_1_1,00.html

2) Ronchi E, Harper D, Taylor A, Halsberger AG. Genetic testing: policy issues for the new millennium. Community Genet 2000;3(4):161-3.

3) Ronchi E. Genetic testing: policy issues for the new millennium. J Biolaw Bus 2001;4(3):34-6.

4) Eurobarometer. Available at: http://ec.europa.eu/research/biosociety/public_understanding/eurobarometer_en.htm

5) Final report of the Temporary Committee on Human Genetics (A5-0391/2001). Available at: http://www.europarl.europa.eu/omk/sipade3?PUBREF=-//EP//NONSGML+REPORT+A5-2001-0391+0+DOC+PDF+V0//EN&L=EN&LEVEL=2&NAV=S&LSTDOC=Y

6) European Parliament Report on the Commission communication Life Sciences and Biotechnology- A Strategy for Europe. A5-0359/2002. Available at: http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//NONSGML+REPORT+A5-2002-0359+0+DOC+PDF+V0//EN

7) JRC Report. Towards quality assurance and harmonisation of genetic testing services in the EU". Available at: http://www.jrc.es/home/pages/detail.cfm?prs=1124
8) Ibarreta D, Elles R, Cassiman JJ, Rodriguez-Cerezo E, Dequeker E. Towards quality assurance and harmonization of genetic testing services in the European Union. Nat Biotechnol 2004;22(10):1230-5.
9) Statement by the European Group on Ethics in Science and New Technologies on advertising genetic tests via the internet. Available at: http://ec.europa.eu/european_group_ethics/docs/statgentest_en.pdf
10) Opinion on the ethical aspects of genetic testing in the workplace. Available at: http://ec.europa.eu/comm/european_group_ethics/docs/avis18EN.pdf
11) McNally E, Cambon A, et al. 2004 Report on the ethical, legal and social aspects of genetic testing: research, development and clinical applications. Available at: http://europa.research/conferences/ 2004/genetic/report_en.htm
12) Human genetic testing, what implications? Available at: http://ec.europa.eu/research/conferences/2004/genetic/index_en.htm
13) Progress Reports (2003-2005). Available at: http://ec.europa.eu/biotechnology/progress_reports_en.htm
14) Bioethics. Available at: http://ec.europa.eu/research/biosociety/bioethics/documents_en.htm
15) Draft Guidelines for Quality Assurance in Molecular Genetic Testing. Available at: http://www.oecd.org/dataoecd/43/26/37103271.pdf
16) Eurogentest. Available at: http://www.eurogentest.org/
17) Cassiman JJ. Research network: EuroGentest—a European Network of Excellence aimed at harmonizing genetic testing services. Eur J Hum Genet 2005;13(10):1103-5.
18) Hayhurst R, Cassiman JJ.. EuroGentest standing up to scrutiny—first year demonstrates good progress harmonizing community approaches. J Appl Genet. 2006;47(1):5-7
19) Public Health Genomics European Network. Available at: http://www.phgen.nrw.de/typo3/index.php
20) Brand A, Schroder P. Public health genetics - experiences and challenges. Community Genet. 2006;9(1):5-7.