

Regulating DTC genetics: an overview of global trends

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What's the problem?

DTC genetics has become a focus for the broader debate about the regulation of genetic testing

Policy options

What is the existing regulatory landscape?

- Regulation of medical devices
- Laboratory accreditation
- Codes of practice and clinical guidelines

Where are the gaps?

1. Failures in our medical device regulations

- Variety of loopholes in different jurisdictions (esp. LDTs)

2. Failures in our clinical lab regulations

- Many countries lack comprehensive statutory framework for regulation of clinical laboratories.

3. Other issues

- Aspects of DTC services may not be covered by regulations for medical devices or clinical laboratories

DO NOTHING



and hope it will go away

**MAKE
IT
ILLEGAL**



SET SOME RULES



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**ENFORCE
THE RULES**



Regulatory options

1. International treaties/standards (e.g. OECD)
2. National legislation on genetic testing (e.g. Germany)
3. Reform of IVD device regulations (e.g. Australia)
4. Codes of practice (e.g. UK and Japan)
5. Enforcement of consumer protection laws (not covered here)

Option one

International treaties/standards

- OECD Best Practice Guidelines for Quality Assurance in Molecular Genetic Testing (2007)
- Council of Europe Convention on Human Rights and Biomedicine (1997) / Additional Protocol on Genetic Testing for Health Purposes (2008)

OECD Guidelines

Context

- Organisation for Economic Cooperation and Development
- 30 member states
- Collects and analyses data and provides forum for exchange of ideas and policy development including international guidelines
- Active in health, biotechnology, biomedical innovation
- 2003 survey on genetic testing
 - International trade in samples
 - Lack of uniformity in laboratory quality assurance
- Work on quality assurance guidelines
 - Initiated 2003, completed 2007

OECD Guidelines

Molecular genetic testing should be:

- Delivered within healthcare framework
- Practised under a quality assurance framework
- Comply with applicable legal, ethical and professional standards

OECD Guidelines

Informing the patient

- counselling should be available (proportionate + appropriate)
- test results should be reported to referring healthcare professional
- Advertising, promotional and technical claims ... should accurately describe the characteristics and limitations of the test offered.
- Laboratories should make available to service users current evidence concerning the clinical validity and utility of tests they offer.

OECD Guidelines

Implementation by member states

- Survey in 2008
 - 13 member states responded
 - Most responding countries indicated they had either implemented the guidelines or were preparing to do so
- OECD will be carrying out a survey to assess what is happening, evaluate the utility of the guidelines and to review whether any changes needed

Council of Europe

- Established 1949
- Intergovernmental organisation fostering cooperation amongst its 47 members to protect democracy and human rights
- Active in bioethics since 1980s
- Convention on Human Rights and Biomedicine (1997)
- Additional Protocol concerning genetic testing for health purposes adopted by Committee of Ministers in 2008
 - First internationally legally binding instrument concerning health-related genetic testing

Council of Europe

Additional Protocol on Genetic Testing (2008)

- Clinical utility should be an essential criterion for a test to be offered
- Parties shall take the necessary measures to ensure that genetic services are of appropriate quality. In particular, they shall see to it that:
 - a) genetic tests meet generally accepted criteria of **scientific validity and clinical validity**
 - b) a **quality assurance** programme for laboratories including regular monitoring
 - c) persons providing genetic services have **appropriate qualifications**

Council of Europe

Additional Protocol on Genetic Testing (2008)

Art. 7 Individualised supervision

- 1) A genetic test for health purposes may only be performed under **individualised medical supervision**.
- 2) **Exceptions** to the general rule referred to in paragraph 1 may be allowed by a Party, subject to appropriate measures being provided ...

However, such an exception may not be made with regard to genetic tests with important implications for the health of the persons concerned or members of their family or with important implications concerning procreation choices.

Council of Europe

Additional Protocol on Genetic Testing (2008)

Art. 8 Information, genetic counselling and consent

2) For **predictive** genetic tests as referred to in Art. 12 of the Convention on Human Rights and Biomedicine, **appropriate genetic counselling** shall also be available for the person concerned. The tests concerned are:

tests predictive of a **monogenic** disease

tests serving to detect a genetic **predisposition** or genetic **susceptibility** to a disease

tests serving to identify the subject as a healthy **carrier** of a gene responsible for a disease.

Council of Europe

Current status of Additional Protocol

Entry into force requires ratification by five states including four member states

So far only five members states have signed the protocol but only one member state has ratified it

NB some key member states have not signed or ratified the main Convention on Human Rights and Biomedicine

Option two

National legislation on genetic testing

Austria

Gene Technology Act 1995

- Regulates GMOs, genetic testing and gene therapy
- Predictive genetic testing – special lab requirements, pre- and post-test counselling, written informed consent
- Part IV, Section 65
 - Genetic testing may only be carried out where it is at the request of a doctor specializing in medical genetics

Belgium

Royal Decree 1987

- Restricts genetic services to small number of centres
- Sets various standards including need for pre- and post-test counselling (offered on a non-profit basis)
- All genetics centres must produce annual reports detailing their activities

France

Decree no. 2000-570: Articles R1131-4 of the Public Health Code

- Standards for laboratories
- Restrictions on labs which can perform testing
- Need for informed consent and medical supervision

French Bioethics Law 2004

- Gave regulatory powers to Agence de la Biomédecine
 - Authorises institutions permitted to carry out PGD
- Current debate on renewal of 2004 Bioethics Law

Germany

Genetic Diagnosis Act, 2009

- Prohibits genetic discrimination
- Requires laboratory accreditation
- Informed consent and counselling
- Diagnostic genetic examinations may only be conducted by medical doctors and predictive genetic examinations may only be conducted by medical doctors with specialist genetics training
- Establishes independent Genetic Diagnostic Commission
 - Develop guidelines
 - Review new developments in science/technology

Norway

Law No.56 1994 : Act relating to the Application of Biotechnology in Medicine

- General guidelines for research on embryos, gene therapy and genetic testing
- Institutions undertaking these activities must report regularly to the government
- No restrictions on diagnostic genetic testing
- Presymptomatic/predictive/carrier testing
 - cannot be carried out on minors
 - must be accompanied by pre- and post-test counselling
 - Confidentiality restrictions

Portugal

Law No.12/2005 Personal Genetic Information and Health Information Law

- Restricts use of genetic data, forbids discrimination
- **Carrier, presymptomatic and susceptibility testing** must be preceded by genetic counselling and written informed consent, and requested by a medical geneticist (does not apply to diagnostic/PGx tests)
- Counselling should be **proportionate** to the severity of the disease, usual age at onset and existing treatment
- Full implementation of law awaiting final decree

Sweden

Law 114, 1991 - on gene technologies within the context of general medical examinations

- Focuses on genetic screening
- Organisations wishing to carry out testing must have authorisation from the national government
- Additional guidelines on PGD published in 1995
 - Restricted to diagnosis of progressive, hereditary diseases which may lead to death and for which there is no cure/therapy

Switzerland

Federal Act on Human Genetic Testing 2004

- Informed consent, privacy etc.
- Organisations wishing to carry out testing must have federal authorisation
- Genetic tests may only be prescribed by medical doctors (or under their supervision)
- Presymptomatic and prenatal genetic tests and tests for the purpose of family planning may only be prescribed by doctors who have received appropriate postgraduate training ... and must be provided with pre- and post-test non-directive counselling

South Korea

- Advisory committee convened by Korean Society of Medical Genetics review common DTC tests with funding from Ministry of Health and Welfare
- Since 2007 14 genetic tests banned and six restricted
 - Banned include tests for obesity, diabetes, alcoholism
 - Restricted include BRCA, APOE
- DTC genetic tests are prohibited
- 2005 – Korea Institute of Genetic Testing Evaluation established with support of government
 - Quality assurance and evaluation of clinical validity

Common themes

- Restrictions on
 - who can perform testing
 - who can order testing
 - How test data can be used
- Standards for how genetic testing is performed
 - Quality assurance
 - Protection of privacy
 - Informed consent
- Genetic information is special, but some is more sensitive
 - Predictive testing
 - Prenatal testing

Questions

- Are DTC genetics companies complying with national legislation?
- Does such national legislation affect cross-border trade?
- Is there any evidence of enforcement activity?
- Are clinical standards applicable to rare disease testing appropriate for susceptibility or pharmacogenetic testing?
 - Is counselling necessary and if so how much is “proportionate”?
- Does the specialist expertise of healthcare professionals trained in clinical genetics give them particular competence to deal with susceptibility testing?
- Does requiring a doctor’s involvement stop bad tests?

Option three

Reform of IVD regulations

- Australia
- European Union

EU device regulations

IVD Directive

- Most tests (including genetic tests) classed as **low-risk** so **no independent pre-market review**

EU device regulations

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- LDTs performed outside EU are not covered
- Clinical validity or just analytic validity?

The IVD Directive: beyond a joke?

Interviewer:

“What do you think of the European regulations?”

Company:

“We like them; there aren't any [laughs].”

Interview with leading US molecular diagnostics company, 2006

Review of IVD Directive

Issues raised in European Commission consultations (2008/9) include:

- Adoption of new risk classification system
 - GHTF model – pre-market review for genetic tests
- Revision of essential requirements
 - Clinical validity, clinical utility
- Clarification of status of LDTs
- Special measures for DTC genetics

Australia's new IVD regulations

Restrictions on IVDs for self-testing (home use)

IVDs intended for self-testing are tests that are used in the home or a similar environment and are not carried out under the supervision of a health care provider. Certain types of self-testing IVDs will be prohibited from supply.

These include:

- IVDs used to test for pathogens or diagnose notifiable infectious diseases
- tests to determine genetic traits
- IVDs used to test for serious disorders, for example cancer or myocardial infarction.

Australia's new IVD regulations

- All LDTs are medical devices
- High-risk tests reviewed by TGA
- Low and moderate-risk tests
 - labs must register with TGA
 - labs must notify TGA when tests introduced
 - test validation carried out by bodies responsible for lab accreditation - NATA and NPAAC

BUT

- TGA participate in standard setting
- TGA can intervene where there is a concern

Option four

Codes of practice/guidelines

- Japan
- UK

Japan

- 2005 - guidelines on protection of individual genetic information published by Ministry of Economy, Trade and Industry
- 2006 – companies establish the Consortium for the Protection of Individual Genetic Information
 - encourage compliance with 2005 guidelines
 - 2008 - publish QA guidelines based on OECD model
- 2008 – JSHG publish comments on DTC genetic tests

UK

Code of practice and guidance on human genetic testing services supplied direct to the public, September 1997

- Laboratory accreditation
- Confidentiality of data
- No testing of minors
- Provision of counselling
- Information about test, its scope and limitations, and the accuracy, significance and use

UK: ACGT code of practice

Tests where DTP was acceptable

- Carrier status for inherited disorder where an abnormal result carries no significant direct health implications for the customer

Tests where DTP was discouraged

- Inherited dominant and X-linked disorders, chromosomal disorders, for adult onset genetic disorders regardless of inheritance, **or for the genetic component(s) of multifactorial diseases including tests for somatic mutations**

UK: after the ACGT, the HGC

Genes Direct: Key recommendations

- Pre-market review of tests as medical devices
- No statutory ban but some tests should not be offered DTC – esp. *predictive*
- Code of practice
- Discourage DTC advertising
- Stricter controls where adverts are allowed
- Public education campaign
- Funding for independent information source

Beyond *Genes Direct*

- *More Genes Direct* (2007)
 - Reasserts key recommendations from *Genes Direct*
 - International meeting to discuss a code of practice 2008
 - Industry represented : DNA Direct, deCODE, Navigenics, 23andme, Genetic Health, BIVDA
 - Overwhelming support for code
 - Value of a quality mark
 - Risk stratification to determine regulatory approach
- BUT
- Minimum standards should apply to all tests
 - Consent, confidentiality, laboratory QA

Guiding Principles

- Working group formed in 2009
 - included Navigenics and deCODE
- to develop *guiding principles*
 - High-level overarching document which could apply across jurisdictions as basis for codes of practice
- Public consultation (international)
 - Wide divergence of views on what categories of tests should be DTC
- Final document published in 2010

Guiding Principles

- Tests for inherited/heritable disorders require pre- and post-test counselling
- Other tests may also be best delivered with medical supervision - need to consider:
 - Severity of condition
 - Reliability of prediction
 - For progressive diseases – likely speed of degeneration
 - Impact on clinical management
 - Impact on tested individual
 - Familial implications
 - Potential for test to provide genetic information about a fetus
 - Availability of confirmatory tests
 - Impact on personal relationships/family stability

What next for UK?

- Human Genetics Commission is now being wound up
- No move in UK to transpose principles into a code of practice
- UK may be unique in world in having diminished its regulatory control over DTC genetics

BUT

- HGC remained committed to view that a code of practice was only part of the regulatory solution, DTC genetic tests also needed to be treated as IVD devices and subject to pre-market review

Conclusions

- Number of countries imposing legal restrictions on DTC genetics has increased at same time as number of companies offering DTC genetic tests has grown
- Rule-making activity is not matched by enforcement activity
- This may change if DTC market grows

But that is a big IF

- Sustainability of DTC business model is unproven
 - Companies are struggling e.g. Sciona closure, deCODE bankruptcy, lay-offs at 23andme
 - Companies are supplying to physicians e.g. DNA Direct, Navigenics

Has the train already left the station?



We're still laying the rail tracks



Let's try to avoid disaster



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Further useful information:

<https://www.eshg.org/270.0.html>

See also (not fully up-to-date but still very useful):

<http://www.nature.com/ejhg/journal/v11/n2s/full/5201111a.html>