



Genetic Testing

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Scope and framework

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General framework

- Lots of documentation regarding ethical/legal aspects on genetic testing
- Here we consider genetic tests that have an interest for health or for research
- Other applications exist or are developing
- Much information on a website of an EU funded FP6 network of excellence : EUROGENTEST (www.eurogentest.org)

What's at stake?

“...the rapid pace of change has produced two powerful, but conflicting, social reactions. On the one hand, there is very strong public support for breakthroughs promising better medical diagnosis and treatments...; on the other, there are anxieties about increased loss of privacy and the potential for genetic discrimination, as well as about the capacity to regulate genetic science in the public interest.”

Essentially Yours: The Protection of Human Genetic Information in Australia, Australian Law Reform Commission, 2003.

Issue of definition (1)

- According to Additional Protocol to the Convention on human rights and biomedicine concerning genetic testing for health purposes
 - « Tests which are carried out for health purposes, involving analysis of biological samples of human origin and aiming specifically to identify the genetic characteristics of a person which are inherited or acquired during early prenatal development. »
- This does not cover research, does not cover genetic tests on human embryo/fœtus.

Issue of definition (2)

- A broad definition was used by an EU expert group for genetic testing, i.e. “*any test that yields genetic data*”. Genetic data or information relate to inherited or acquired properties that are transmitted during cell division and that affect subsequent generations of offspring (“*germinal genetic data*”) or cells and tissues (“*somatic genetic data*”).

Issue of definition (3)

- OECD
- *“Genetic testing is testing for variations in germline DNA sequences, or for products/effects arising from changes in heritable sequences, which are predictive of significant health effects.”*

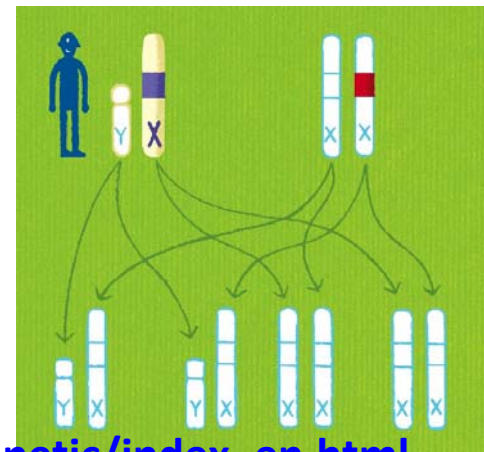
Trends for definitions

- First recommendation from an EC expert group in 2004
 - Call for internationally agreed definitions
 - Work towards a consensus
 - Explicit the definition used in each official document
- Tendency is to include samples and data under the term of database or biobank
- Lexicons and attempts to initiate interoperability through a common understanding of terms



EUROPEAN
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Community Research



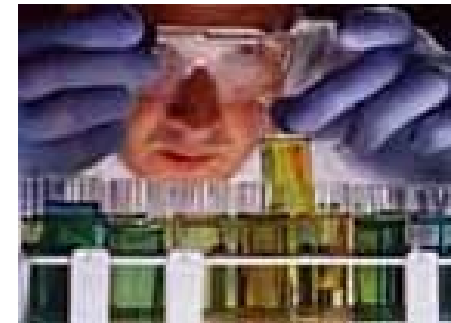
http://europa.eu.int/comm/research/conferences/2004/genetic/index_en.html

Comment at: <http://www.ircm.qc.ca/bioethique/obsgenetique/>

*The report +
25 Recommendations of the EC
Expert Group on the Ethical,
Legal and Social Implications of
Genetic Testing*

*Conference on Human genetic testing: what
implications?*

Brussels, May 6-7, 2004



Genetic exceptionalism : dangerous with good intentions...

- Exceptionalism vs specificity
 - Genetic exceptionalism : « the belief that the particular nature of genetic information gives rise to greater risks that are different from other health risks» (EC Expert Group report, 2004)
 - Genetic data/database specificity: « the consideration that the double dimension of genetic information, as personal data, inherited and transmissible, and as contribution to a common human heritage has implications for their use and regulation » (proposal)

Guiding principles

- Human dignity
- Human rights and fundamental freedoms
- Autonomy
- Privacy
- Non-discrimination and non-stigmatization

International texts and guidelines

- Nuremberg Code (1947).
- Helsinki Declaration (1964 - 2002).
- Directives from WHO. (Manille, 1981-).
- *Statements HUGO (1996 -)*.
- *UNESCO Declaration (1997 -)*.
- *UNESCO Declaration (2003)*
- Convention of Council of Europe (Oviedo, 1997).
 - *Additional protocol on genetic testing for health purposes (2008)*
- Recommendations ESHG (2001 -).
- Declaration of principles for research in genetics and in population genetics (Quebec, 2000 - 2002)
- National ethics committees working since 1995

Universal Declaration on the Human Genome and Human Rights, UNESCO, 1997.

- Need to address ethical issues of genetics (preamble)
- Genome – common heritage of humanity (art. 1)
- Respect individuals' uniqueness and diversity (art. 2)
- Non-commodification of the human genome (art. 4)
- Benefit-sharing (art. 12)
- Freedom of research (art. 12)
- Solidarity (art. 17)
- International co-operation (arts. 18, 19)
- The Universal Declaration is a starting point; it is now up to the States to put the Declaration into practice...

Extract of UNESCO International Declaration on Human genetic data (2003) Art. 4

(a) Human genetic data have a special status because:

- (i) they can be predictive of genetic predispositions concerning individuals;*
- (ii) they may have a significant impact on the family, including offspring, extending over generations, and in some instances on the whole group to which the person concerned belongs;*
- (iii) they may contain information the significance of which is not necessarily known at the time of the collection of the biological samples;*
- (iv) they may have cultural significance for persons or groups.*

(b) Due consideration should be given to the sensitivity of human genetic data and an appropriate level of protection for these data and biological samples should be established.

Extract of UNESCO International Declaration on Human genetic data (2003) Art. 5

Purposes

Human genetic data and human proteomic data may be collected, processed, used and stored only for the purposes of:

(i) diagnosis and health care, including screening and predictive testing;

(ii) medical and other scientific research, including epidemiological, especially population-based genetic studies, as well as anthropological or archaeological studies, collectively referred to hereinafter as “medical and scientific research”;

(iii) forensic medicine and civil, criminal and other legal proceedings, taking into account the provisions of Article 1(c);

(iv) or any other purpose consistent with the Universal Declaration on the Human Genome and Human Rights and the international law of human rights.

The variety of genetic data and databases (1)

– Genetic data

- Individual level (e.g. pharmacogenetics)
- Familial level (e.g. monogenic genetic disease)
- Populational level (e.g. multifactorial diseases)

Susceptibility data vs presymptomatic diagnostic

– Genetic epidemiology designs (patient, family or population based)

- shape the biobank/database contents

The variety of genetic data and databases (2)

- issues at stake and tendency in their regulation
 - **Degree of identifiability**: double coding favored
 - **Informed consent**: large consent tendency
 - **Withdrawal**: allowed if no irreversible anonymisation
 - **Secondary uses**: to be considered as a realistic option
 - **Public engagement and trust**: major factor but how?
 - **Return of results to persons**: general or individual?
 - **Dissemination of results, risks and stigmatisation**: anticipate
 - **Commercialization and benefit sharing**: explicitation + notion of common good

Binding/non binding texts

- The additional protocol to Oviedo Convention will be binding when signed and ratified
- Some countries have laws that specifically regulate genetic testing
- Guidelines from international institutions (OECD, UNESCO)
- Professional guidelines (ESHG)
- Ethics committees opinions

Some of the issues

- Right to know and not to know
- Return of results (research) and delivery of information (health care)
- Protection of confidentiality
- Production of mass genetic information
- Sharing of research data and results
- Research and clinical care sometimes mixed up

(a) Right to know

“No one should be denied access to his own genetic data...”

UNESCO (2003) art. 13.

“Personally identifiable information ... should be subject to adequate subject access rights”

WHO (2003) rec. 18.

“...after the completion of the study, subjects will be informed of the finding of the research in general, and individual subjects will be informed of any finding that relates to their particular health status”

CIOMS (2002) Guideline 5(7).

Right not to know

“... the person concerned has the right to decide whether or not to be informed of the results”

UNESCO (2003) art. 10.

“Adequate account must be taken of the privacy interest that individuals have in not knowing information about themselves.”

WHO (2003) rec. 16.

New developments, new issues

- Research developments bring new questions or challenge the existing frameworks
 - GWAS and Whole genome studies
 - Caulfield T, McGuire AL, Cho M, Buchanan JA, Burgess MM, Danilczyk U, Diaz CM, Fryer-Edwards K, Green SK, Hodosh MA, Juengst ET, Kaye J, Kedes L, Knoppers BM, Lemmens T, Meslin EM, Murphy J, Nussbaum RL, Otlowski M, Pullman D, Ray PN, Sugarman J, Timmons M. ***Research ethics recommendations for whole-genome research: consensus statement.*** PLoS Biol. 2008 Mar 25;6(3):e73.
 - Issues of public release, for example

Ethical issues in genome screen approaches

- Numerous markers might immediately or later on, in case of long term analyses, reveal information on other conditions than those that are the object of the study : issue of incidental findings and public release become major.
 - How to handle such potential information must be foreseen.
- Issues of re-identification
- Sharing of data and samples

Issues of the future (1)

- **Duty to Recontact:**

- Who, if anyone, has the duty to return results? Is there a “chain of obligation”

- **Right to Withdraw**

- degree to which there is an ethical requirement to structure the research and dissemination of results in a manner that will allow the right to withdraw to endure as long as possible

Issues of future (2)

- **Risk/Benefit Analysis**
 - need for a comprehensive risk/benefit analysis of public data sharing
- **Governance Structures**
 - need to systematically evaluate existing and emerging governance structures

An example of recent questioning

- The open policy for sharing data challenged by new situations due to technological development

NIH GWAS data sharing policy challenged by scientific advances

- A research team, led by David W. Craig, Ph.D. at the Translational Genomics Research Institute (TGen) in Phoenix AZ, has developed *a new bioinformatics method that allows the detection of a single person's SNP profile in a mixture of 1,000 or more individual DNA samples*
- *Homer et al., PLoS Genet 2008 4(8): e1000167. doi:10.1371/journal.pgen.1000167* : “Resolving Individuals Contributing Trace Amounts of DNA to Highly Complex Mixtures Using High-Density SNP Genotyping Microarrays.”
- In other words, bioinformatics techniques have progressed to the point that with enough genomic data on an individual from another source, it is now possible to determine whether that individual participated in a study by analyzing only the pooled summary data.

Adaptation

- This discovery, however, has important policy implications for the way the scientific community shares such pooled sets of genetic data.
- Because individual SNP profiles can now be detected within aggregate data, the NIH has moved quickly to assure continued protection of research participant privacy in genomics studies by controlling access to pooled datasets.
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Back to GMP to GBP

- The practices in industry are not disconnected from the general scientific evolution in the domain and from societal reactions
- The clear aim and the quality of tests are indispensable
- Clinical utility to be assessed as a paramount element for introducing into the health systems