

GENETIC RESEARCH – GENETIC PRIVACY

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1. Introduction

The past few years have witnessed a very quick development of biotechnologies and genetic research coupled with a significant growth in the so-called "biobanks", which are being used to an increasing extent both in Europe and in other continents [Pizzeti].

The developments made possible by technologies related to genetics have already an impact, which promises to be more substantial, on health systems and health care delivery. Their impact also has the potential to influence health economics.

The gene has acquired a symbolic status that would appear to be independent or in some way detached from its scientific meaning [Kakuk]. As this metaphor of a "future diary" well illustrates, genetic is surrounded by exaggerated expectations.

Like any medical progress, developments in genetic testing are accompanied by new societal, ethical, economic and health policy questions [EC-25Recommendations]. Genomic approaches are mentioned as the most exciting development over the next years – at the same time genetic research was mentioned as the most worrying development [Meade].

Genetic research involves human biological samples, which raises traditional concerns about patient privacy and informed consent. Yet unlike research on human biological samples, population genetic research is focused on genetic samples, and the nature of genetic information creates an additional layer of complexity by introducing an array of interests from multiple groups that generate novel ethical, social and legal implications [Hsieh]. A major problem seems to be the impact on or even the threat- to the privacy of donors

2. From traditional to genetic research and biobanks

Traditional research with biological specimens generally involves single researchers or established groups, who obtain and use the samples in defined ways to research in discrete areas [Rothstein]. Initially the people actively involved in DNA collection were researchers seeking genetic markers for a particular disease, who typically collected DNA samples from families at risk for the disease of interest and stored those samples [Roche/Annas]. Traditionally researchers obtain informed consent from each research subject to use his or her samples and, where appropriate, an authorisation to obtain, use and disclose the subject's health information

Genetic research activities have recently undergone nothing short of a small revolution. Biobanks have existed for decades in clinical and research settings, but new analytical and computational technologies make it possible to utilize these extant repositories and to develop new biobanks for a range of biomedical research activities. Many sample collections have left their traditional home or a small refrigerator in a laboratory to reach the unprecedented proportion of large, sophisticated storage centers containing DNA samples from whole populations [Deschenes/Sallee]. In the post-genome world of high throughput gene sequencing and computational biology, biobanks hold the promise of facilitating large-scale research studies. Biobanks are repositories of human biological materials collected for biomedical research [Rothstein]. The term biobank is used variably to designate several types of collections of biological samples as well as the collections of personal -genetic or other - data referring to the persons, whose biological samples are included in a biobank.

The uses of human genetic material in biobanks is very variable. Samples can be used in population genetics research, identification of the genes playing a role in a specific disease, or clinical research and development of pharmacogenetic tests. [EC-25Recommendations]. What these data collections have in common is the combination of health and lifestyle data with human bodily substances and genetic information for the purpose of researching complex diseases [Mund].

There are a large number of major projects involving researches into the most common diseases of civilisation of our time. One of the best-known projects is without doubt the Icelandic Biobank, operated since 1998 by a private pharmaceutical company, deCode Genetics and set up with government support. Other examples of population based biobanks include the Estonian Genome Project, launched by the Estonian government in 2001, as well as the UK Biobank [Mund].

Biobanks represent a new paradigm of biomedical research. Population biobanks raise new ethical issues because they introduce a new approach to epidemiology in an attempt to quantify the role of multiple genetic and environmental factors in population health. However, the separation of ethical debates regarding population biobanks from concerns about their scientific validity and underlying assumptions about health has a number of important consequences and has been criticised [Wallace].

DNA banking is quickly changing from an academic research activity to a governmental and commercial enterprise conducted by DNA brokers. In the case of biobanks the individual or entity obtaining the sample may not be engaged in research, but may only be a broker or intermediary supplying specimens to other researchers. The purpose of a biobank is to develop a repository that can be used for many research protocols, often in numerous research areas. A biobank contemplates future research activities, including research by investigators who cannot be specified at the time of sample collection. As a result the relationship between subjects and

researchers is being severed and along with it legal rights and obligations to reduce risks to subjects' privacy and to maintain the confidentiality of their information [Roche/Annas].

3. Does genetic research affect genetic privacy?

Scientific and technological developments in human genetics and the enhanced opportunities for gathering all genetic information on individuals in "big containers" go hand in hand with the increase in business, financial and commercial interests focused on these very peculiar data. Fundamental values and principles of civil society such as freedom, privacy and personal identity are bound to be touched upon [Pizzeti].

It has been widely observed that the nature and degree of risk of biobank research depends on the identifiability of the sample and any linked health information and on whether the samples are extant or to be collected prospectively [Rothstein]. Research with identifiable samples raises the risk that there will be an invasion of the sample donor's privacy.

There are numberless definitions of privacy: privacy is like an elephant, is more readily recognized than described. Privacy can only be defined meaningfully in terms of the cultural norms of a particular society and the position of individual within the society.

Privacy can be viewed as a state of non access to the individual's physical or psychological self. Privacy can also be seen as a state of non-access from others – informational privacy. The rights of the individual, as the source of the material, cannot merely be translated into his/her right to confidentiality and to privacy, but must also encompass autonomy and free choice [EC-Recommendations]

The concepts of liberty, autonomy and privacy are interrelated. Indeed we can go so far to say that they are interdependent, each relying on the other to fulfill its true function in the most effective way possible. It is impossible to make autonomous choices without a degree of freedom from interference and consequently to truly free or fully autonomous without some element of privacy. Each of these concepts performs the same function, albeit in different ways: each represents an expression of the fundamental respect that a liberal, democratic society has for its citizens [Laurie] and in this context privacy is strictly related to dignity [Rodota].

4. Genetic privacy and genetic data: a specific category?

There was no such concept as genetic privacy before scientific advances provided us with the means to gather and manipulate genetic information. Privacy is challenged by the increased availability of genetic information [Laurie]. The creation of computerised databanks facilitates the rapid processing and manipulation of data and as such represents another potentially significant source of harm through use

and misuse of information – in particular the establishment of genetic databanks has given rise to particular concerns and calls for specific protection. A further problem from the data protection perspective concerns the transmission of data and/or samples to third parties, outside the research environment [Mund].

A first question, strictly related to the extent and the protection of privacy, is the nature of genetic information. Is genetic information a sub-category of health information? Health or medical data, i.e. qualify as “sensitive personal data” and, as such, they receive more stringent protection, permitting processing only in limiting circumstances. Or, is genetic information unique, as it also reveals information about our heritage and connections to relatives and communities? The basic nature of genetic data is exactly that they can supply information going well beyond identification data, as it has to do in particular with health, ethnic origin and kinship.

The Council's of Europe Recommendation No R (97) 5 on the protection of medical data, i.e. a non-binding legal instrument (and for the purposes of this recommendation) has defined medical as well as genetic data. The notion of medical data refers to all personal data concerning the health of an individual. It refers also to data which have a clear and close link with health as well as to genetic data. Under the terms of the recommendation, "medical data" should also include any information - unless it is public knowledge - giving a ready idea of an individual's medical situation, for instance for insurance purposes, such as personal behaviour, sexual lifestyle, general lifestyle, drug abuse, abuse of alcohol and nicotine, and consumption of drugs. This was the reason for including in the definition of medical data the words "manifest and close", i.e. having a clear and direct impact on the health situation of the individual. The expression "genetic data" refers to all data, of whatever type, concerning the hereditary characteristics of an individual or (concerning) the pattern of inheritance of such characteristics within a related group of individuals. It also refers to all data on the carrying of any genetic information (genes) in an individual or genetic line relating to any aspect of health or disease, whether present as identifiable characteristics or not.

Genetic research is frequently portrayed as though it will reveal the essence of humanity and unlock the secrets of our destiny and who we are as human beings. The general public as well as academics, politicians and legislators already regard genetic information as very sensitive information, belonging to the most intimate realm of the private sphere. The specific nature of genetic information draws on following elements:

- it relates to families and not just individuals
- it can offer a degree of certainty or a measure of predictability in the assessment of likelihood of ill health
- it can reveal secrets about future ill health or determine future risk

The public conception is that genetic information on the individual contain knowledge of some sort of determining rails, which sooner or later will lead the individual to certain, unavoidable harms, problems or even advantages. Many use the term “genetic exceptionalism” to mean roughly that genetic information is so sufficiently different from other kinds of health-related information that it deserves special protection or other exceptional measures.

Such a reductionist view sets too much store by the influence of genetics in the determination of the human condition. Although the aetiology of many diseases might involve a genetic component, genes are neither necessary nor sufficient in themselves to cause the disease itself. On the other side many argue that the predictive value of genetic information is much lower than is usually expected and stress the attention to the fact that also other types of health information have significant implications for family members. Kakuk points out that someone’s DNA is not genetic information in itself. It requires extensive interpretative work conducted by specialists in order to obtain meaningful information that might be sensitive [Kakuk].

The problem of genetic exceptionalism emerged as a crucial issue in deciding how the upcoming information deluge and testing technologies should be regulated. The UK Human Genetics Commission acknowledges in a report, published in 2002, that from a general point of view genetic information is not special, but it is exceptional, because of the cumulative effect it could have in some contexts. The Independent Expert Group of the European Commission acknowledges in a Report appeared in 2005 that the fear of abuse and misuse of genetic information is genuine. However, it feels that these institutional responses to this fear are inappropriate, as abuse and misuse can also occur, and has occurred (example HIV) with any other medical information.

The Group acknowledged that without doubt a perceived policy tendency to place medical genetic data apart from other medical data is based on strong and noble goals to assure the protection of human rights against the dangers of genetic discrimination, genetic determinism and the violation of genetic privacy. However the Group underlines that initiatives aimed at regulating genetic data separately from general medical data would create major practical problems in health management, since it would be impossible to clearly differentiate between what is medical and what is genetic data. While some argue that our DNA acts a future diary revealing our genetic secrets, others have pointed to the difficulties of defining genetic information in law and in separating what is genetic, and so deserving of special protection, from what is not.

The Group regards genetic exceptionalism as inappropriate. It does not support the idea of constructing specific islands in policy or regulatory texts that might fragment and jeopardise the development of a core set of rules concerning medical data,

privacy and informed consent, and which might delay, rather than support, the prevention of medical discrimination in general, including discrimination based on genetic testing results.

5. Privacy as protection against discrimination

Discrimination seems to be inseparably connected to possible uses of genetic information.[*Kakuk*] The possibility cannot be ruled out that research results associating diseases with genetic endowment may be perceived as stigmatizing by those concerned and in their social environment. Moreover, research findings indicating that members of certain subpopulations are more likely to have a genotype conferring an increased risk of disease or other traits could lead to stigmatization or discrimination against members of specific population groups [Rothstein].

It is crucial to enquire as to what the real source of genetic discrimination is. It might be the predictive value of genetic tests that enable us to foretell the future health status of a given individual or it might be the social representation of genetic information that is supported by stereotypes, myths and unfounded beliefs regarding the real nature of genetic information. [*Kakuk*]. As the German Ethikrat points out, in its Report concerning Biobanks, this perception reflects an over evaluation of genetic factors that fails to do justice to the significance of other conditions of human life.

The risk of results of genetic diagnosis being used in society to discriminate against people on the grounds of their genetic characteristics must be precluded by statutory regulation of fields in which the relevant information can be used in discriminatory ways, for instance by stipulating restrictions on the use of genetic findings in the sphere of employment and insurance. In this context the protection of privacy and genetic as well as other data becomes a prerequisite for equality and non-discrimination principles [Pizzeti].

6. Consent as element of self-determination

On the whole, the modern expression of autonomy and control over the use of personal data is found in the imperative to obtain consent, which is the first line of defence and the expression of the donor's right to self-determination. The principle of respect for patient autonomy requires that consent be given both for the release of personal information and for the collection of information, for example by testing.

This is also the case in the research context. This means that the collection of bodily substances from his body and the gathering of personal data, in both cases for subsequent use in biobanks for the purpose of medical research must be subject to the donors consent [*Laurie*]. The requirement of consent must also apply whenever samples and data obtained for other reasons – e.g. diagnosis or therapy – are subsequently to be used for research. This kind of multiple sample use is extremely

valuable for medical research but in the past it usually took place without explicit consent.

The requirement of the consent may be waived if the samples and data are completely anonymized. In some countries, under current data protection legislation the requirement of consent may also be waived if the scientific interest in the conduct of the research project substantially outweighs any interest of the donor in exclusion from use and if the purpose of the research cannot be achieved in any other way, or can be achieved only with disproportionate effort and expense.

Consent must always be subject to the furnishing of appropriate information on all circumstances recognizably relevant to the donor's decision. These, as a rule, include:

- the voluntary nature of participation
- the purposes, nature, extent and duration of the proposed use
- the extent of and the conditions for the possible transfer of samples and data
- the possibility of communication of research results to the donor
- information on the possible consequences of the communication of results of genetic analyses for the donor and its relatives, including possible obligations to divulge (.e. to insurance institutions)
- anonymization or pseudonymization of samples and data
- other ancillary donor protection measures
- any provision for State access to samples and data
- the right to withdraw consent

The information need only cover personal risks to the donor arising directly in connection with the use of samples and data in biobanks [Ethikrat].

7. Blanket consent for research?

There is considerable scholarly and professional debate on the necessity, extent or nature of informed consent for biobank research. There are two main issues : First informed consent is broadly required when samples will be collected, stored or released in an individually identifiable form. Second, informed consent depends on whether the samples are extant or prospective.

A first question, which arises, concerns how precise the consent of the data subject needs to be. Depending on the focus, some give priority to either the autonomy of the

donor or the research interest for practicality and implementability of the research projects. Specific consent protects the individual from the risks of unknown research that could potentially lead to adverse consequences.

Based on a respect for individual autonomy, specific consent allows the individual to have control over the use of his/her sample. Many argue that the scientific potential of biobank samples and data can often be fully exploited only if their use is not confined to individual research projects specifiable in advance.

Another factor to consider is that it is not always possible to predict the potential developments in research over time. [EC-25 Recommendations]

With regard to genetic databases, the value of the information lies in its potential use for multiple research purposes. Genetic information is useful for the study of all types of diseases, and the organization of a large amount of data will be a powerful source for regression analyses.

Together, genetic population databases have the potential for multiple uses inside and outside the research arena, and ethical debates center on whether consent may be given for a broad purpose that leaves open the possibility that the data sample can be used again in a different type of research.

A “blanket consent” would make it possible for the biobank to use samples and data for every type of research – even for research, which was not foreseeable at the time consent was given. The UK Biobank has adopted the principle of “blanket consent” and the German National Ethics Council has indicated its support for a blanket consent system for Biobanks, provided that the consent can be withdrawn at any time [Ethikrat].

People who provide their tissue for genetic research have strong interests in controlling its future uses. Traditionally such interests have been safeguarded by the doctrine of informed consent.

A failure to restrict the scope or the duration of the consent runs counter not only the data protection principle of proportionality but also the principle of transparency and purpose limitation. However the conflicting regulation of informed consent has led to chaos and the proliferation of biobanks increases the need for new comprehensive approaches [Rothstein].

A solution could be that donors should have the possibility of excluding their samples from certain types of research [Mund]. Biobank administrators and lawyers should be able to draft an informed consent document with sufficient specificity to inform potential donors of the possible intended uses. The document could describe a range of possible uses of the specimen, with the risks and benefits of each one, and then seek a single consent for all uses.

8. Anonymization and monitoring

Proponents further contend that if such samples are anonymized, no ethical issues are raised because there is "no breach of confidentiality, of duty to communicate results, of risks of stigmatization or of discrimination" [Hsieh].

Once donor data have been entered into the biobank, the next question that needs to be addressed is the anonymization and/or the encoding of data.

To protect donor privacy, when biobanks samples and data are stored and used, personal information allowing inferences as to donor identity shall as far as possible be concealed at least by coding [Ethikrat]. Certainly anonymisation of data or samples can go so far in protecting the interests of the persons to whom they relate and it can influence the ethical appropriateness of gathering and using samples and data, because the risk of harm through misuse is reduced.

Absolute anonymity is achieved when no means are available to link data to an identifiable individual. "Proportional" or "reasonable" anonymity exists when no reasonable means of identification of individual is possible. It is generally accepted that proportional anonymity of samples or personal data is sufficient to comply with international standards of anonymisation [Laurie].

Various degrees of identification/ anonymization of the individual sample donors are possible: Samples and data can be:

- a) identified,
- b) identifiable (single-coded),
- c) identifiable (double-coded),
- d) anonymized; and,
- e) anonymous.

The ethical and legal issues are different in these various situations. The extent to which informed consent is required can vary depending on the nature of the research, the degree of anonymity, and the question of whether the research may result in new findings of relevance for the (health) care of the donor. Additionally it must be taken into consideration that if data and samples are totally anonymized the rights to withdraw consent or to invoke their right to be informed about the results (the so-called genetic feedback) can no longer be upheld.

Given the open-ended nature of informed consent and the multiple transfer of information, monitoring of biobanks is of paramount importance. Monitoring involves the supervision of the bank's activities in both its scientific (data quality, accuracy,

work processes) and ethical aspects (respect for subject's rights, pertinence of the activities).

As already mentioned, improper management of personal or collective data is one of the main risk related to genetic research. Thus, in addition to implementing measures to physically protect information, the supervision of these measures as well as of their use must be organized.

It is a well-established principle that any research project involving natural persons/beings should be reviewed and approved by an independent ethics review board. This fundamental principle thus applies to population genetic research projects. Monitoring of data protection and security mechanisms have been contemplated by all the projects.

They have attempted to find solutions adapted to both participants and society's demands while ensuring that researchers' freedom is not unduly restrained. Data protection authorities or monitoring bodies, independent from the projects, enjoy the impartiality to act and be perceived as appropriate ombudsmen guaranteeing participants' protection and projects' adherence to the strictest and highest standards of data protection.

Public biobanks are often controversial and the oversight mechanism established with the biobank plays an important role in ensuring the credibility of the enterprise. Public confidence in the aims of research and the motivation of researchers has been undermined in recent years. An additional factor is the rise in the role and control of the private sector in medical research, which has been met with a great deal of scepticism on the part of the public [Laurie].

Such oversight will serve to maintain the biobank's credibility and the trust of the population that research is being conducted to maximize the potential benefits and minimize the potential harms arising from the repository. Credible and efficient mechanisms of accountability and transparency should be built in the creation and management process of such projects and should be clearly defined ahead of time. They constitute key components of the consent process and will prove to be the cornerstone of a successful long-term research legacy [Deschenes/Sallee].

9. Conclusion

Genetic research and mainly the establishment of biobanks for research purposes raises new challenges worldwide for the legislator in terms of protection of donors' data and personality rights.

If such biobanks unquestioningly represent progress in medical research (and by implication in public health) ethical issues such as consent, privacy and the role of commercial companies become issues that must be managed and addressed in ways that win public acceptance and allow the biobank to go ahead as planned.

Debates on privacy, consent, feedback and intellectual property are influenced by research decisions regarding what data are needed and by whom; what information is likely to be learned about participants during the course of the research; and when participants need to be re-contacted to update or collect new data. Unless these scientific decisions are examined critically, ethical debates can be based on false assumptions [Wallace].

When weighing up the different interests in connection with biobanks, the interest of research cannot be dismissed. The risks of infringing donors' personality must not be trivialised either. It is important that the sensitivity of collected donor data be included in the equation [Mund].

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