# 1 Introduction: some lessons of ELSAGEN

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The investigation of ELSAGEN (Ethical, Legal and Social Aspects of Human Genetic Databases: A European Comparison), which was funded by the European Com-mission from 2002 to 2004, was occasioned by plans to construct population-wide databases in the four participating countries: deCODE's database in Iceland, the Estonian Genome Project, UK Biobank and Medical Biobank of Umeå in Sweden. Interdisciplinary research teams – with scholars and students from philosophy, law and sociology – were formed at ethics centres of six universities in these four countries: the University of Iceland, which coordinated the project, Tartu University in Estonia, Lund University in Sweden and the Universities of Central Lancashire, Lancaster and Oxford in the United Kingdom. This research also benefited from the network 'The Ethics of Genetic and Medical Information', financed by the Nordic Academy of Advanced Study (NorFA, now NordForsk) from 2002 to 2006.

This research, therefore, concerns databases which are new or under construction and which will collect information specifically for the intended multi-disease and population health research. A human population genetic database is a collection of genetic, medical and, in some cases, genealogical data from a large number of people, arranged in a systematic way so as to be searchable.[1] As a rule, such databases are intended to provide data for research in human genetics and medicine, exploring interaction between genes, lifestyle, environmental factors and health and diseases. They are mainly non-clinical databanks in the sense that the aim is not to gain information about individuals for clinical intervention but to obtain general knowledge about diseases and to improve health and health services. More specifically, the aim of the research is to identify genes linked to common diseases and to the regulation of drug response as a basis for drug development. Some of the databanks are also intended for clinical use where the aim is to gain data

[1] See HUGO Ethics Committee, 'Statement on Human Genomic Databases', 2002.

about individual participants and inform them about their health risks and possible ways to deal with them (for example, the 'gene card' in Estonia). There are different sets of ethical questions at issue in the cases of clinical vs. non-clinical databanks: ELSAGEN concentrated on the latter, i.e. on issues concerning the collection, storage and use of data mainly intended for genetic epidemiology and pharmaceutical research.[2]

The ELSAGEN research project had two major objectives: (I) to anticipate and address questions raised by recent developments in genetics research by providing knowledge of ethical, legal and social aspects of population-based human genetic databases; and (II) to consult citizens in order to gain knowledge of public views of privacy and related moral values in the context of human genetic databases.

The main theoretical tasks of the project can be divided into five categories: (1) empirical mapping, i.e. finding out what are the actual policies and people's concerns regarding human genetic databases in the four countries; (2) interpretive, comparative analysis of existing laws, policies and views; (3) conceptual analysis of the basic categories in the moral discourse about databases, such as privacy, consent, discrimination and social benefits; (4) critical analysis of arguments, laws, policies and views that have been put forth or voiced concerning these issues; and (5) finally, establishing how existing ethical frameworks and social policies reflect people's concerns and how they need to change in the light of new scientific and technological developments.

In order to deal with these theoretical tasks and to reach the objectives of ELSAGEN, five workpackages were formed. The following is a brief description of these workpackages and a summary of the main lessons to be learned from them. The main results of the research work are described in the individual sections of this book.

1. A Workpackage on National and European Values was divided into (i) an empirical survey which was to provide knowledge about public views on privacy concerning human genetic databases, people's trust in public and commercial organizations with regard to the collection and storage of personal data, and to what extent these views and attitudes vary between the four countries; and (ii) bioethical analysis of the results.

   Some of the most significant results from the empirical survey concern people's perception of the trustworthiness of professionals and institutions. Not surprisingly, previous experience of gene technology

[2] For a general discussion of ethical and legal aspects of databanks, see e.g. B. M. Knoppers (ed.), *Populations and Genetics. Legal and Socio-Ethical Perspectives* (Leiden: Martinus Nijhoff, 2003).

seems to shape citizens' views and concerns in this respect. Thus there is generally more trust in genetic science and scientists among Estonians and Icelanders than there is in England. If people feel that they can trust scientists and institutions, they seem to be willing to further genetic science and believe that it will improve their health and welfare even though in many cases they do not claim to understand the issues. The bioethical implications of the survey are discussed specifically in the concluding chapter of this book.

2. A Workpackage on Social Issues was divided into (i) governance – analysis of the exercise of political, economic and administrative authority in the management of databases; (ii) discourse on databases – analysis of the public discourse on the databases, studying the types of arguments used in the debates; and (iii) social justice – analysis of conceptions and applications of social justice in relation to the databases.

   It is striking that none of the four databanks that were the focus of the research are in operation, at least not according to the plans that were the focus of the ELSAGEN research. Although genetic databank research in Iceland is thriving, the Icelandic HSD project has stalled. The Swedish company UmanGenomics has ceased operating, and the plans in the UK and Estonia are still in (slow) progress.[3] There are different reasons for the slowness or lack of progress in each case, which cannot be discussed here, but the general lesson is that public consultation is an important factor that should be undertaken early in the process. It is time-consuming but crucial for building trust among prospective participants. This requires an extensive informed public debate in time to feed into the policy- or law-making processes. Another important lesson for governance is that political authority and regulation should be kept independent of the commercial interests that most often need to be harnessed in order to finance the projects. This separation is an important precondition for trust, and it requires careful thought about the relationship between community ownership and commercial interests. Finally, on the issue of social justice, there is a tension between global and local relevance. As Chadwick and Wilson have pointed out, while global arguments are used for their implementation, the benefits of databases may reside in their local relevance.[4] Other research has shown that people are motivated by the

[3] The Medical Biobank of Umeå is still functioning, however.
[4] R. Chadwick and S. Wilson, 'Genomic Databases as Global Public Goods?', *Res Publica* 10 (2004), pp. 123–134.

vision that all population groups get equal access to research results.[5] Benefit-sharing discussions need to take account of these complexities as both the justifications and the responsibilities for benefit-sharing change when a local research context is switched to one where concerns of global justice become relevant.[6]

3. A Workpackage on Law was divided into (i) collection of data on laws, regulations and other relevant documents; (ii) analysis of common issues and problems; and (iii) issues such as privacy, consent, responsibility, ownership and access to information which were scrutinized in view of developing a normative framework.

   An important lesson from the legal research is that there is a striking lack of standardized guidelines, and this inhibits co-operation among researchers in this field, even at the European level. The research also revealed a need to map the landscape of population databases and to distinguish in legislation between different kinds of databases and database research. National legislation about human population databases is partly based on misleading paradigms, and such databases are not always covered by the legislation. One problem is that legal definitions do not adequately reflect current practice. This fact points towards the importance of consulting scientists or facilitating dialogues between them and ethical, legal and social scholars about these issues. It is also important to consult the public, of course. The concluding chapter of this book deals with the question of how the law reflects the concerns of the citizens as they appear in the empirical survey.
4. A Workpackage on Ethical Issues was divided into (i) privacy – a conceptual analysis of privacy and an ethical analysis of issues of protection of personal genetic and medical information; (ii) consent – a conceptual analysis of consent and an ethical analysis of issues of consent of participants in population-based human genetic databases; and (iii) genetic discrimination – an ethical and conceptual analysis of the issue of possible genetic discrimination in the context of population-based human genetic databases.

   In the minds of the public, privacy seems to be closely related to trust. It is essential for trust that people have good reasons to believe that their privacy is protected. Even though the main emphasis in the discussion has often been on coding techniques and legal technicalities, there will

[5] K. Hoeyer, T. Mjörndal, B.-O. Olofsson and N. Lynöe, 'Informed Consent and Biobanks: A Population-Based Study of Attitudes Towards Tissue Donation for Genetic Research', *Scandinavian Journal of Public Health* 32 (2004), pp. 224–229.

[6] See K. Simm, 'Benefit-Sharing: An Inquiry Regarding the Meaning and Limits of the Concept in Human Genetic Research', *Genomics, Society and Policy* 1, 2 (2005), pp. 29–40.

also be instances in the process where participants have to rely on traditional confidentiality as a professional moral requirement. This is one of the reasons why trust is a crucial matter and also why the professional integrity of the scientists must not be forgotten in the discussion. In her chapter on trust, Margit Sutrop argues that it is important to avoid both blind trust and irrational mistrust in building up support for databases. Trust needs to be based on critical reflection on the competence and goodwill of those trusted and it needs to take into account possible risks related to database research.

People seem also to connect privacy with control of information. However, human population databases are poorly equipped to allow participants much individual control over information once it has been stored. If participants have good reason to believe that they can trust the institutions which regulate the research, the people who work with the information and also the technical system which protects it, the issue of privacy should not be a major obstacle in the effort to balance participants' interests and scientific research interests. A key precondition for this trust is that information will under no circumstances be handed to parties who might be motivated to use it against the participants, such as employers or insurance companies.

This issue relates to the issue of discrimination, which is a major concern of the public. Lena Halldenius argues that the standard account of discrimination needs to be reconsidered in order to account for and effectively prevent genetic discrimination, which requires a strong public health system and strict regulation of private health insurance. Building trustworthy overseeing institutions with transparent and reliable guidelines also serves a major role in ensuring public trust. Participants must be correctly informed about the use of their data and assured that they will only be used for the medical research purposes initially consented to. Non-deception is a precondition for both trust and voluntariness.

Privacy also relates directly to the question of consent for participation in database research because, generally, there is an inverse relation between the stringency of privacy requirements and the emphasis on consent. Anonymization of data (so that it is made irretrievably unlinkable) obviously increases protection and may thus lessen the need for consent, but it also reduces possible research and medical benefits. Since databases are basically resources for research, the data stored in them are mainly intended for (at least) secondary use. Therefore, it is impossible to foresee the exact use of data for research at the time of collection. This creates a particular challenge for the ethics of database research.

The discussion in ELSAGEN was, naturally, oriented towards the particular databases that were under construction in the participating countries and took account of the experiences of them. The emphasis was on the need to find a middle ground between open, unrestricted consent and standard, specified informed consent. It is proposed that participants would be asked to authorize the use of their data for described healthcare research that is foreseeable at the time of collection and for comparable research permitted by research ethics committees. This authorization, which can be regarded as an explicit consent to clear conditions for use, protection and regulation, is in the spirit of informed consent, but it is more general and open.[7] It is argued, however, that such authorization, for participation in research on data that have been collected in human genetic population databases of the type discussed in the ELSAGEN research, meets the moral demands of respecting the person of research participants and provides sufficient grounds for voluntary choice and for regulation that respects that choice.

5. Finally, a Workpackage on Knowledge, Values and Human Rights was divided into (i) fundamental concepts – analysis of the fundamental concepts of bioethics and their relation to human genetic databases; (ii) effects on ethical frameworks – an ethical analysis of how ethical frameworks mutate and change in the light of new technologies; and (iii) database sciences in context – a critical analysis of the social, historical and philosophical context of the science and technology on which the human genetic databases are based.

   The upshot of the analysis of fundamental concepts in bioethics is that the widely accepted 'American' principles of respect for autonomy, protection from harm and observance of justice, paired with their 'more European' counterparts of respect for dignity, precaution and solidarity, are of major importance in the ethical discussion of databases. As Matti Häyry has argued, bioethical principles 'should be employed to promote discussion, not to suppress it' and 'it does not really matter where they came from, if they can be used to promote sensible bioethical discussion'.[8] Respect for dignity and autonomy is fleshed out in responsible procedures of privacy and consent. Protection from harm is a major responsibility of ethical review boards. Observance of justice comes primarily to rest in the procedures for

[7] For an argument along these lines relating directly to the Icelandic case, see V. Árnason, 'Coding and Consent. Moral Challenges of the Database Project in Iceland', *Bioethics* 18 (2004), pp. 39–61.

[8] M. Häyry, 'European Values in Bioethics: Why, What, and How to be Used?', *Theoretical Medicine and Bioethics* 24 (2003), pp. 199–214, at p. 199.

protecting vulnerable research subjects and in the fair distribution of benefits of the research.

In this context it is crucial to note that the existing ethical frameworks for research were primarily formed either for the type of research where there is a direct physical participation, such as in clinical trials, or for more traditional epidemiological and statistical use of data. Participation in genetic database research is of another kind and raises separate questions for ethics and governance. The legislation, governance and ethical regulation of these new kinds of databases must reflect their specific and various research uses and purposes and take into account the experience of the scientists who have been involved in database research practice. Information technology, for example, has not only enabled the construction of these databases but also provided us with new and effective means of keeping participants informed. This offers participants ways of checking the use of data and facilitates dynamic opt-out procedures. Two of the chapters in the section on political considerations are thus on the impact of biobanks on ethical frameworks and on the issues of governance.

Finally, even though much emphasis is laid in this book on actual public concerns and existing legal regulations, it also takes on the theoretical task of critically analysing the cultural context of genetic science and technology. We are entering a new era of multifaceted commercialized databases that have been enabled by an enormous growth in genetics in combination with advanced computer technology. As a consequence, the traditional research ethos is in a state of upheaval and we are facing new challenges. It is important to address people's concerns, but they are often not based on good information about these complex issues and they are largely influenced by genetic ideology. Therefore, empirical mapping, legal interpretation and conceptual analysis must be complemented with a critical examination of the science and technology on which human genetic databases are founded and of the prevailing social discourse. The chapters by Piia Tammpuu and Gardar Árnason are analyses of such discourse which often furthers interests other than those of the public and the research participants.[9] However, a strong protection of these latter interests, as well as informed public discussion and scientific literacy, is a precondition for the possibility of human population databases becoming a genetic wealth of nations.

[9] On this point, see also V. Árnason, 'Sensible Discussion in Bioethics: Reflections on Interdisciplinary Research', *Cambridge Quarterly of Healthcare Ethics* 14 (2005), pp. 322–328.

*Part I*

# Background

# 2 On human genetic databases

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Human genetic databases have the primary purpose of providing data for research in human genetics and medicine. They combine health data and genetic data from a large population, and include in some cases genealogical information or lifestyle information.

The authors of this volume focus on four human genetic databases in as many countries: the Medical Biobank of Umeå in Sweden, deCODE's Health Sector Database in Iceland, the Estonian Genome Project and UK Biobank. To date only the first of the four has been established, but it has had serious operational problems. The Estonian Genome Project and UK Biobank are slowly progressing, but deCODE's plans to establish a health sector database appear to be on hold.

The Medical Biobank of Umeå is owned and operated by the University of Umeå and Västerbotten county council. The University and the county council founded together the company UmanGenomics,[1] which is responsible for the commercial uses of the biobank. The biobank is based on a cohort study of cardiovascular disease and diabetes, which have a relatively high frequency in the county of Västerbotten. Since 1990 residents of Västerbotten county have been invited for a health check-up when they turn forty, fifty or sixty. They have been invited to donate blood samples to the biobank, which has resulted in a database with about 100,000 samples (about 70% donated by participants in the study, the rest donated by participants in other studies) which is growing by about 5,000 samples each year. Information about health and lifestyle is also collected from participants.

The Swedish Medical Research Council drew up detailed ethical guidelines for biobanks in 1999. Informed consent is sought from all participants, both for inclusion of data in the database, and, in principle, for individual studies. A research ethics committee can allow the use of data for studies without requiring informed consent under certain conditions,

[1] See UmanGenomics' website at www.umangenomics.com.

for example if the new study is sufficiently similar to previous studies where informed consent has been given, or if no personally identifiable information is used.[2]

deCODE's Health Sector Database is to be owned by the Icelandic state, but established and operated, through an exclusive licence, by deCODE genetics Inc., a biotechnology company incorporated in Delaware, USA, but based in Iceland.[3] The database is to include data from medical records from the Icelandic population, and the data can be temporarily cross-referenced with genetic data and genealogical data. The database is expected to include data and samples from about 250,000 participants. Informed consent is to be sought for genetic data, but health data is to be collected from medical records unless the individual 'opts out' by signing an opt-out form. Genealogical data is considered public information and no consent is required for its inclusion in the genealogical database.[4]

A Supreme Court decision in 2003 allowed close relatives of a diseased person to prevent data about that person being entered in the Health Sector Database. This Supreme Court judgment requires changes to the current laws on the Health Sector Database, but a new bill does not seem to be on the horizon. The Icelandic database project appears therefore to be on hold.[5] Nevertheless deCODE genetics Inc. has established both a genetic database with around 100,000 samples and a comprehensive genealogical database about the Icelandic nation. Information about health and lifestyle is also collected from participants and the company is doing research on various diseases.

The Estonian Genome Project aims to collect health and genetic data from up to 1 million Estonians. The database will be owned by the state, but operated by the Estonian Genome Project Foundation, a non-profit organization established by the Estonian Government.[6] The Estonian

[2] See A. Abbott, 'Sweden Sets Ethical Standards for Use of Genetic "Biobanks"', *Nature* 400 (1999), p. 3; A. Nilsson and J. Rose, 'Sweden Takes Steps to Protect Tissue Banks', *Science* 286 (1999), p. 894; Swedish Medical Research Council (MFR), 'Research Ethics Guidelines for Using Biobanks, Especially Projects Involving Genome Research', adopted by the Swedish Medical Research Council in June 1999 (Dnr 1999–570).

[3] See deCODE's website at http://www.decode.com.

[4] V. Árnason and G. Árnason, 'Informed Democratic Consent? The Case of the Icelandic Database', *Trames* 8 (2004), pp. 164–177; V. Árnason, 'Coding and Consent. Moral Challenges of the Database Project in Iceland', *Bioethics* 18 (2004), pp. 39–61.

[5] R. Gertz, 'An Analysis of the Icelandic Supreme Court Judgement on the Health Sector Database Act', *SCRIPT-ed* 1:2 (2004), http://www.law.ed.ac.uk/ahrb/script-ed/issue2/iceland.asp.

[6] The information about the Estonian Genome Project is from its website, http://www.geenivaramu.ee, and the website of the Estonian Genome Foundation, http://www.genomics.ee.