Biobank Governance: Trends and Perspectives

H. Gottweis^a K. Zatloukal^b

^aDepartment of Political Science/Life Science Governance Research Platform, University of Vienna, Vienna, and

^bInstitute of Pathology, Medical University of Graz, Graz, Austria

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Abstract

Biobanks are a challenge and topic for governance. Today, biobanks are identified as a biomedical scientific/infrastructural development that warrants a political/legal/ethical reaction with the goal to integrate biobanks into the preexisting fabric of regulation, medicine, law and society. Biobank governance is always a response to sociocultural challenges and requires the building of trust, acceptance, and careful political negotiation. Biobanks are regulated in networks of governance in which the state is one actor next to others, and the ordering and structuring of the interaction between biobanks, society, and politics operates through a variety of actors, on different levels and along particular rationalities. Such networks of governance reflect, to some extent, a post-regulatory state in which governance has become a complicated architecture and field of action involving a multitude of forces and rationalities. Biobank governance is still a relatively new field of political-legal intervention and it will be crucial for the future of biobanks to establish governance regimes that appropriately link research with society and politics.

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Introduction

In recent years, biobanks have become a major strategic issue in the field of biotechnology and genomics. Biobanks are collections of biological material including associated data. This article refers exclusively to biobanks containing human biological samples which are established within the healthcare system and the medical sciences. Some European countries consider basically any inventory or archive of biological material is a biobank [1], whereas in other countries biobanks are seen a major research infrastructure. Biobanks come in many different forms according to the type of samples that are stored and the medical-scientific domain in which they are collected. Clinical settings, research projects and the judiciary field are typical sites for biobank collections [2].

Biobanks gained prominence when, a few years ago, a number of countries and health providers initiated large population-based studies in order to identify genes contributing to complex diseases and to study the interaction of genetic and environmental factors in the etiology of disease. Companies involved in biobank projects, such as Iceland's deCODE Genetics, have become known worldwide to mass publics, and its CEO, Kari Steffanson, turned into an icon of the new medical genomics industry. Like deCODE, most major European biobanks, such as GenomEUtwin, Karolinska Biobank, Estonian Biobank, UK Biobank, EPIC, KORA, LURIC, the Danubian Bio-

bank Consortium have a focus on blood and blood-derived DNA. Therefore, most experience and literature refer to or, at least, have a focus on blood or DNA biobanks [3]. In contrast, tissue banks are far less in the spotlight. This is because most tissue banks were established in a fragmented manner, resulting in collections of variable size, composition, standards and with different goals [2, 4, 5]. However, hundreds of millions of human tissue samples are stored in pathology archives all over the globe, a fact which receives increasingly regulatory and public attention, this is partially related to the prominence of population database projects and partially due to a general new trend in ethical-regulatory thinking about human specimens. In several countries, such as in Great Britain, Iceland, Sweden, Spain, France and Austria, there are already large, well-organized biobanks or tissue repositories representing huge populations. In addition, some countries have an advantage by large historical tissue collections that go far back in time. For example, in Norway alone, 15–20 million tissue samples have been collected for diagnostic purposes dating back to the 1930s. Similar patterns of collection can be seen in Germany and Austria, in particular located at pathology institutes.

The current, rapid developments in the building, connecting and optimizing of biobanks are not only of crucial importance for research, industry and the medical system, but they have also raised a number of ethical, social and political issues, which have led to controversy and conflict in some countries. Especially prominent is an interconnected set of issues around the questions of informed consent, personal integrity, self-determination, confidentiality and non-discrimination that has played an important role in the current debates about biobanks. In fact, it is not exaggerated to state that these key themes of ethics and bioethics have occupied the central place in the current public and political-regulatory debates on biobanks. In public discourse – and academic literature – the central challenge in the creation and operation of biobanks seems mainly to be how to deal adequately with potentially conflicting issues such as self-determination and confidentiality. The key question, as it appeared in public and expert discourse, was: how can the setting up and, more generally, operation and development of biobanks be combined with securing that humans continue to be protected in their rights and dignity? [6] Today, such considerations apply to both the relatively spectacular large population genetics databases such as in Iceland or UK Biobank, but also to the many tissue collections as they exist all over the world, typically in hospitals.

Thus, biobanks are identified as a biomedical scientific/infrastructural development that warrants a political/legal/ethical reaction with the goal to integrate biobanks into the preexisting fabric of regulation, medicine, law and society.

This integration has not always proven to be easy. Biobank governance is by no means a complete success story. Despite manifold attempts to govern the newly emerging field of biobank development, so far the political history of biobanks, in particular of population-based genetic databases, was fraught with controversy, resistance and often fruitless attempts to create regulatory structures for biobanks on a national level. The increased public-political attention that is being paid to human genome research, and the collection of biological materials has also increased pressure for biobanks that have hardly received much public attention in the past, such as tissue collections established in the context of histopathological diagnostic service to reconsider their regulatory practices and strategies. Biobanks have turned out as rather unruly phenomena, the governance of biobanks has remained a heterogeneous patchwork operating through mostly local guidelines, codes of good practice, and national ethics regulations, and any biobank operator today is faced with a number of different, partially new governance challenges.

Biobanks ‘Old’ and ‘New’

Despite the fact that biobanks have only recently received much public and political attention, they are not something new in the world of medicine and biological research. The systematic collection of human cells and tissues has been done for many years even dating back to the 19th century, including formaldehyde-fixed and paraffin-embedded as well as frozen viable and non-viable material. In some countries, as well as in Europe, millions of tissue samples are being permanently stored, for example in pathology institutes. However, more recently large patient registries and population surveys were initiated to enable the linking of biological and genetic data with general patient data, which triggered the public debate.

Currently, several European countries are establishing large biobanks with prospective collections of biological material and health data from the donors. Most prominently, in 1998, the Icelandic Ministry of Health had announced its plans for the construction of a Health Sector Database on the entire Icelandic population. These plans,

initiated by the private company deCODE Genetics, specified how and under what conditions to assemble medical records and, if possible, combine them with genetic data and genealogical records for the purposes of tracking the presumed genetic bases of diseases and economizing the National Health Service. The founding premise of deCODE Genetics was that the family has proved to be a useful unit in the study of monogenic disorders. For complex or 'polygenic' disorders, which are caused by mutations in a variety of genes and are strongly influenced by genetic polymorphisms as well as lifestyle and environmental effects, large families and well-defined cohorts (population isolates) are needed. deCODE researchers reasoned that a Health Sector Database might be useful in this context. Although information on DNA, medical data, and genealogical records would only be combined in the context of specific research projects, monitored by ethics committees and public officials, their synergistic coexistence was supposed to enhance each other's economic and medical value [7].

But Iceland's approach towards biobanking was unique in strategy and context. Practices for collecting biological materials and related data differ widely from institution to institution, and the coordination between different biobanks varies. Enormous potential exists for health research when comparing freshly collected cell and tissue samples to old archived material, provided that the analyses give comparable results [2]. In several countries, such as in Great Britain, Iceland, Scandinavian Countries, France and Austria, there are already large, well-organized biobanks or tissue repositories representing huge populations. For most of this period there are good epidemiological registries for different diseases, especially in cancer [1].

Basically, four large types of biobanks are distinguished in the literature: (1) Clinical case/control biobanks that are based on biological specimens from patients with specific diseases and from non-diseased controls. Pathology archives typically fall into this group of disease-oriented biobanks. (2) Longitudinal population-based biobanks that contain biological samples from (parts of) the general population with or without disease. Subjects followed over a large period of time are expected to develop different diseases with a certain frequency. The UK and Estonian Biobanks are examples for this type of biobank. (3) Population isolate biobanks, which are characterized by the homogenous genetic and environmental setup of the population represented (e.g., the Icelandic Biobank). (4) Twin registries, such as GenomEUtwin, which contains samples from monozygotic

and dizygotic twins, and, therefore, is particularly suited to distinguish between the genetic and non-genetic basis of diseases. The different biobanks are complementary in the sense that the longitudinal population-based cohorts depend on end-points from clinical case (disease-oriented) biobanks, both for precise delineation of phenotypes and for molecular characterization, based on genomics, transcriptomics, proteomics or metabolomics analyses. On the other hand, for etiologic research questions, the researchers working with disease-oriented biobanks will need control subjects and biological material that have been collected at an earlier time point as part of the longitudinal population-oriented cohorts. In recognition of the synergy potential of biobanks, the establishment of international networks of bio(tissue)banks has been assigned a very high strategic priority not only to cover the emerging demands for such resources but also to increase efficacy in medical genomics and to reduce research costs [3, 8, 9].

Thus, the emerging landscape of biobanks worldwide is hardly a phenomenon of local interest, and a clear realization in the life-science community exists that the creation of worldwide biobanks networks and cooperation will constitute a crucial step in rebuilding the genomics/postgenomics apparatus of modern biotechnology. The policy vision behind this development is that the exploitation of biobanks and registries at the European level during a period when recent improvements of large-scale research in cell and molecular biology will enable new possibilities for health research, knowledge production, and understanding of causes, progression, prognosis and treatment of different diseases [10]. Ultimately, biobanks might be an important step towards the improvement and development of preventive, genetic, and 'personalized' medicine. In fact, in some countries, such as Japan, the biobank projects are seen as 'implementation' of the idea of 'personalized medicine', understood as the development of new, 'tailored' drugs based on the study of diseases and drug side effects, made possible by biobanks and genetic research. In other countries, biobanks were defined as machines of innovation policy. In Estonia, for example, the preparation and establishment of the Gene Bank was funded by investors through the limited company EGeen which was granted exclusive commercial license. But the Estonian Genome project was construed as more than just a large research project; it was defined as a way of pushing Estonia's post-Soviet economy towards Western standards. In Estonia there is a constant search for Estonian Nokia. Typically, every now and then something is regarded as being new 'Nokia'.

The Estonian Genome Project has not been an exception. It figured prominently in the government's Research and Development Strategy 'Knowledge-Based Estonia' 2002–2006, according to which the government foresees knowledge-based development as the main challenge for the long-term competitiveness of Estonia. The potential opportunities presented in the strategy relate to the preconditions of the knowledge-driven economy: the development of human resources, the strengthening of relationships between industry and science, the promotion of high-tech development and its integration with more traditional industries, the stimulation of internationalization, and an intensification of investment into R&D. The three key areas of development include biotechnology and biomedicine, user friendly IT, and material technologies. In this context, the strategic position of the Estonian Biobank project did not even depend on its success. It was argued that whether the EGP succeed or not, the value for money in terms of publicity in international media would be far greater than the costs for the public sector. The more biobank projects such as in Estonia and in the UK turn into 'national projects', the more pressure mounts to develop appropriate regimes of governance.

Biobank Governance: Scientific, Ethical and Political-Regulatory Perspectives

Despite many similarities, the 'early' biobanks as developed in Europe during the 1930s had very different operational and scientific goals than the current biobank projects. Pathology collections had, just as today's population biobanks, a strong interest in identifying and understanding diseases, but, for example, medical doctors in the 19th century Habsburg monarchy, like the pathologist Carl von Rokitansky and the Viennese Medical School had a very different approach towards disease than, for example, Swedish medical doctors at Umeå Hospital have today.

Two major areas of life science development have led to an increasing interest for the idea to create biobanks, the methodological breakthroughs in molecular biology and proteomics with all their impact on the practice of medical research, and the developments in IT science and bioinformatics and their impact on the possibilities to handle large data volume and the systematic collection of material from large populations. These transformations and their application potential raise completely new sets of issues and sensibilities for biobank governance. For example, while the donation of blood or tissue samples for

a specific research project or collection at first sight does not pose any significant problems for the obtaining of informed consent, the development of large biobanks, and, in general, the speed of development in molecular biology and their many potential utilizations of these samples raises the difficult question of how to obtain consent for such a multitude of possible research purposes. Likewise, the treatment of confidentiality in the context of the ever more complex, larger biobanks poses difficult sets of questions. The protection of information is one of the most sensitive issues and remains an issue of great concern for the public and their attitudes towards biobanks. Of particular importance is how biobanks prevent possible misuse of data for discrimination by employers and insurers.

A further new topic of contention in the context of biobanks is issues of ownership, patenting and commercialization. In Iceland, deCODE Genetics received the license to construct the genetic database, in return for a fee paid to the medical service. A rival biotechnological company, UVS, was established in the heat of the debate on the Health Sector Database, partly to challenge deCODE's 'monopoly' of biomedical research in Iceland. Much of the discussion of the database project in Iceland focused on issues of property, ownership, and control. The arguments of the proponents of the Icelandic project tended to emphasize the opportunities it provided in terms of medical advances, work, entrepreneurship, and private initiative, in the age of the challenging 'new economy' and stagnant or declining fishing stocks. A fundamental debate developed concerning the ownership of and access to genetic information and medical records. For many of the critics, the commodification of biomedical data was problematic. The dominant focus in the debate was the fact that a private multinational company positioned itself to explore the genetic bases of common diseases in the entire Icelandic population and to commercialize its results [7].

Many of the core questions of biobank governance are also focused on the ethical dimensions of biobanks. Indeed, a vast part of the literature dealing with questions of biobank governance tries to think together a number of central principles of bioethics with contemporary trends in biobank development. The current discussion in bioethical discourse, the issues of informed consent, personal integrity, self-determination, confidentiality and non-discrimination play a major role. Here the challenge is to balance competing interests, in particular between the interests of science and the involved donors [11]. Ethical practices and regulations vary from country

to country, but converge on some basic principles: informed consent, the protection of participant privacy, and adopted strategies to deal with information related to the collection, be it genetic information or other disease/risk-related information. Connected to the implementation of these principles are other key regulatory questions, such as the issue of disclosure or non-disclosure of result from research projects to individuals. The adoption of standard operation procedures and good scientific practices as well as the creation of an ethics advisory board are elements in such a strategy of ethical governance. Furthermore, the question of ownership and of financial gains from the biobank needs to be dealt with.

For the field of genetic databases, Cutter et al. [12] have identified two basic models of biobank governance: first, legislatively created and regulated projects, such as the Icelandic Act on Biobanks establishing the framework for the Icelandic biobank, or the Estonian biobank, projects created specifically by statutes and related instruments; second, self-created/self-regulated projects, like UK Biobank that are created independently from legislation, and interact with existing laws as the situations arise and that are regulated in a self-binding, but not necessarily legally binding manner. In both cases the issues of the establishment and operation of the biobank, the collection, handling, and access to samples, the relationships with participants, research users and society are regulated through regulations, principles, and ethical guidelines, dealing with issues such as informed consent and confidentiality. Such attempts to govern biobanks develop before, while, or after new biobank projects are considered, created and launched, depending on the factors such as the preexistence or the new creation of genetic collections. In both cases the government or institutional actors close to the state operate as regulators that intend to ensure a sound interaction between biobanks and society. But it is important to see that most of the regulation of biobanks, old and new, is currently based on reports and recommendations of national and international advisory bodies. Internationally harmonized regulations with binding character do not exist [11].

Furthermore, biobanks governance is also increasingly characterized by its deterritorialized, transnational/global character, which neither excludes the national character of projects nor a national rhetoric.

In general, increasingly more technological and scientific advancements in medical research are the result of collaboration on a global scale. In the field of biobanks, the structure is currently still dominated by a national branding, such as 'Biobank Japan' or 'UK Biobank'; how-

ever, other projects such as the Icelandic and the Estonian biobank project already display strong transnational features in the financing structure and product development strategy. At the same time, there is much discussion and preparation going on at the transnational and EU level to tie the various biobank projects, the leading protagonists, infrastructures and strategies together in a common effort. The high strategic priority of biobanks within the EU was recently underlined in the roadmap for European research infrastructures, which foresees a research infrastructure for biobanking and molecular resources. Also the OECD is addressing the challenge of international cooperation of biobanks by developing guidelines for a global network of biological resource centers (www.OECD.org). Another prominent example of efforts for internationalization of biobanks is the Public Population Project in Genomics (P3G), a consortium which has been established to facilitate international harmonization on the ethical and scientific level (www.p3gconsortium.org). For many tissue collections the issue of collaboration and exchange also poses pressing regulatory questions. Again, it must be emphasized that these efforts are only in the beginning. The current proliferation and specialization of laws has led to a multiplication of standards and terminology that puts pressure on harmonizing efforts as a precondition for future cooperation, exchange, and scientific interaction.

Conclusions

The emerging topography of biobank governance displays a complicated picture. Ultimately, the success and failure of biobank projects will depend on their integration into the political and sociocultural fabric. Thought not always viewed in that way, answers to the problems of science tend to be answers to sociopolitical problems, needs, and demands. Therefore, biobank governance should not be misunderstood as a mainly technical challenge. Biobank governance is always a response to sociocultural challenges and requires the building of trust, acceptance, and careful political negotiation. Biobank development refers to the emergence of a multilayered biomedical apparatus that introduces new medical knowledge, rationalities and principles of action, a set of novel strategies of practicing medicine, medical research, interacting with patients, and locating patients within the system of health management. In such networks of governance the state is one actor next to others, and the ordering and structuring of the interaction between biobanks,

society, and politics operates through a variety of actors, on different levels and along particular rationalities. Such networks of governance reflect, to some extent, a post-regulatory state in which governance has become a complicated architecture and field of action involving a mul-

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References

- 1 EU Workshop: Biobanks for Health. Optimising the Use of European Biobanks and Health Registries for Research Relevant to Public Health and for Combating Disease. Report and Recommendations. Oslo 2003.
- 2 Cambon-Thomsen A: The social and ethical issues of post-genomic human biobanks. *Nat Rev Genet* 2004;5:866–873.
- 3 Hagen HE, Carlstedt-Duke J: Building global networks for human diseases: genes and populations. *Nat Med* 2004;10:665–667.
- 4 Kaiser J: Population databases boom, from Iceland to the US. *Science* 2002;298:1158–1161.
- 5 Hirtzlin I, Preaubert N, Duchier J, Jansen B, Simon J, Lobato De Faria P, Perez-Lezaun A, Visser B, Williams GD, Cambon-Thomsen A, Eurogenbank Consortium: An empirical survey on biobanking of human genetic material and data in six EU countries. *Eur J Hum Genet* 2003;11:475–488.
- 6 Tutton R, Coorigan O: *Genetic Databases: Socio-Ethical Issues in the Collection and Use of DNA*. London, Routledge, 2004.
- 7 Pálsson G: The web of kin: an online genealogical machine; in Bamford S, Leach J (eds): *Genealogy Beyond Kinship: Sequence, Transmission, and Essence in Ethnography and Social Theory*. Oxford, Berghahn Books, 2006.
- 8 Pearson H: Summit calls for clear view of deposits in all biobanks. *Nature* 2004;432:426.
- 9 Bouchie A: Coming soon: a global grid for cancer research. *Nat Biotechnol* 2004;22:1071–1073.
- 10 Berg K: DNA Sampling and banking in clinical genetics and genetic research. *New Genet Soc* 2001;20:59–68.
- 11 Oosterhuis JW, Coeberh JW, van Veen E-B: Tumour banks: well-guarded treasures in the interest of patients. *Nat Rev Genet* 2002;3:73–77.
- 12 Cutter AM, Chadwick R, Wilson S: Balancing powers: examining models of biobank governance. *J Int Biotechnol Law* 2004;1:187–192.