



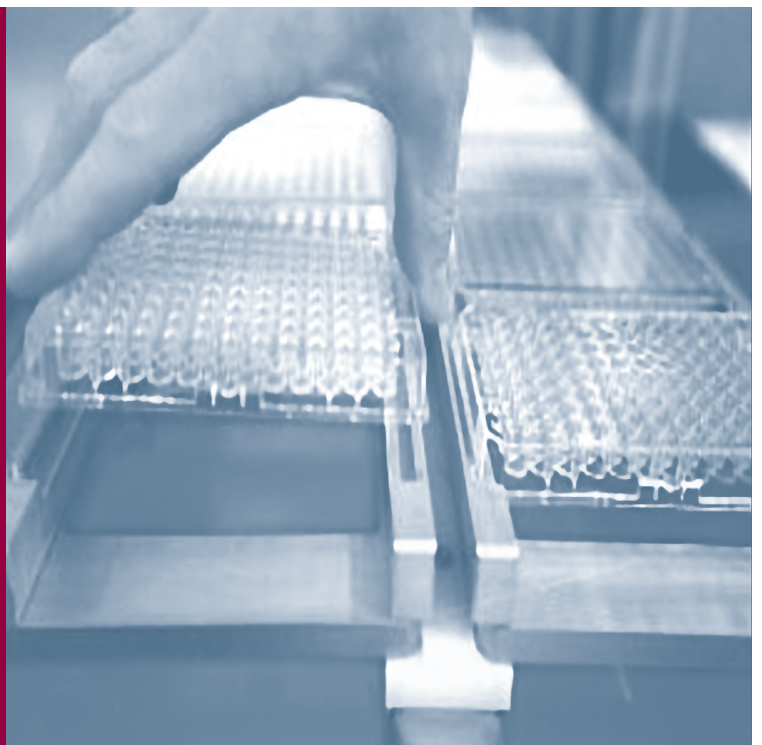
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# Biobanks for human medical research and application

Summary

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## SUMMARY

Biobanks are scientifically set-up collections of samples of human bodily substances (tissue, cells, blood and other materials) as well as DNA, which are established or used in biomedical research. Additional data is often stored along with samples or separate from them, including information about the donor (personal or demographic data, lifestyle-related information, type of illness and course of the disease, and also genetic data). As a result of the growing orientation of medical research on the molecular and genetic level when searching for the causes of illnesses, a new type of bank containing samples and data has come into being. Since the middle of the 1990s these databases have been designated – rather unspecifically – as »biobanks«. The particularity of biobanks lies in their twofold character: Sample collections become important precisely due to the linking of data and information. The extensive and rapid electronic processing of the data and information is also an essential aspect.

In recent years the focus of public attention has been first and foremost on those biobank projects, which have been most comprehensively established, i.e. the (intended) collection of particularly large amounts of data and samples from especially large groups of test persons or donors; where the initiators have specially emphasised the genetic aspect – if necessary with a particular accentuation on future predictions of the probability of falling ill; and/or those which expressed extremely wide-ranging (new) medical opportunities for use as a goal. Such biobanks serve above all as a basis for research on common diseases. The present report concentrates on this type of biobank, at the same time attempting to cover to an extent the diversity of biobanks, and to deal with potential medical applications relating to their scientific significance.

A large number of questions are linked to the development, establishment and operation of biobanks, in particular concerning the collection, storage, use and transfer of samples and data, as well as the social integration of these processes. In numerous countries and institutions biobanks are attracting increasing attention from politics, science, economics and advisory commissions. This is also true of Germany. The potential scientific and medical importance of the subject in particular, but also diverse legal ethical and policy aspects linked to the use of biobanks, prompted the Committee on Education, Research and Technology Assessment to commission TAB with an analysis of this issue.



The present report

- > includes a systematic, overall review and characterisation of the existing biobanks in Germany and discusses the experience gained from large-scale biobank projects using selected international examples;
- > takes the description and characterisation of the different approaches and uses of biobanks as the starting point for a discussion of the scientific significance of biobanks including their integration into research and health policy strategies and development measures;
- > analyses legal, ethical and policy questions related to the establishment and operation of biobanks in Germany (Europe);
- > provides a prospect of the courses of action available for German policy-makers and discusses these with an eye on the general need for clarification.

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## INSTRUMENTAL AND HETEROGENOUS

In Germany, as is also the case in many other European and non-European countries, both on a European and an international level, there are large numbers of biobanks each with different characteristics regarding their organisational and legal form and their research practice. In recent years initiatives have been started to develop common standards for the collection of data, the storage and preservation of samples or the type of operation with the aim of coordinating the biobanks currently being established and of linking research on the data. This has partly to do with the central administration of samples, first and foremost however with the solution of statistical, methodical and infrastructural problems. The foundation and operation of biobanks is not subject to a general approval requirement in Germany. Nevertheless demands are being made, which are of essential importance for biobanks in the future.

Generally biobanks in the first instance represent neither a health issue nor the occurrence of an illness – although they are naturally established and operated for treatment purposes – nor special biomedical technologies or targets, but rather constitute a research resource or a research instrument for what are for the most part still non-specific purposes. The present report covers only those biobanks which are at least also used for research purposes. The instrumental character of biobanks requires considerable heterogeneity, among other things with regard to the type of samples and data, but also to the origin, the method of collection, the organisation, the operation and funding, the application and distribution of the samples, and primarily also the use for very different scientific

issues. A classification or categorisation of biobanks beyond these organisational parameters is problematic and for this reason is not dwelt upon in this report.

Biobanks exist with different operating types and different legal structures depending upon the type of enterprise, which may be subject to public or private law. In the national and European sector biobanks are predominantly public. These are mostly institutions which are maintained by hospitals or academic institutions. However there are also biobanks which are privately operated, for example as a registered society or else a private limited company or non-profit-making private limited company.

If biobanks are created by industrial enterprises, these companies are also in charge of the biobank. In the academic environment, biobanks more often originate from the personal activities of one or more scientists. Here the operation is not generally linked to these people, but with the respective universities and hospitals. These provide personnel for collection and processing of the samples as well as premises and funds for storage. The existing infrastructure in these institutions is a guarantor for professional supervision on the one hand; however on the other hand there is also the risk that the biobank will no longer be supported should the university or hospital change its specialist priorities. For this reason efforts are being made to transfer the biobanks to a statutory framework in the private sector, and to ensure their continued existence there with the aid of a suitable legal entity.

Certain criteria are of relevance when looking for a suitable organisational form for the operation of a biobank, for instance that of avoiding lengthy decision-making processes, the trust between researchers and the public (acceptance), the protection of the confidence of the donor/test persons, provisions for protecting the holdings in order to safeguard the samples in case of insolvency, the protection of the data and samples from unauthorised third-party access, a guarantee by the operating institution of the durability of the biobank, a far-reaching warranty for financial independence or economic viability, as well as the possibility of transferring from one legal form to another (e.g. from a research project into an organisation).

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## **BIOBANKS IN GERMANY**

There is a large number of different biobanks in Germany (in the research field), which are organised, administered and funded very differently depending upon their fundamental aims. When looking at the establishment and operation of



biobanks, one focus of attention is on the networks sponsored by the Federal Ministry of Education and Research (BMBF), the so-called Competence Networks in Medicine.

University research facilities, general hospitals, registered doctors, companies and often also patients' organisations are consolidated in competence networks. Like the genome networks, the competence networks refer to economically important diseases, therefore those which are widespread and occasion considerable costs. The competence networks are to provide a structure, in which research results are more quickly and effectively implemented into clinical practice, and by the same token practice-oriented questions can be carried over into research. In this way, the competence available on diseases which are relevant to health policy both in research and care is linked. This should speed up the evaluation of new insights to effectively counter these illnesses and transfer the results from research into care. There is currently a total of 17 competence networks being funded, five on neurological and psychiatric diseases as well as an overarching organisation for research projects on these diseases, the so-called Brain-Net (nationwide brain tissue bank). Four competence networks relate to contagious diseases, three to cancer, a further three to cardiovascular diseases and two to chronic inflammations. Special biobanks are operated respectively within the scope of these competence networks.

### *Popgen*

Information about relative genetic risks can be obtained through the complete retrospective registration of patients in a certain, geographically limited area. The PopGen project (the abbreviation stands for »population genetics«) is pursuing this approach in the northern part of Schleswig-Holstein with the goal of investigating common diseases. All of the roughly 1,700 medical practices and 41 hospitals in the region are participants in the project based at Kiel University. In close co-operation with clinical partners from the National Genome Research Network (NGFN), PopGen is carrying out the registration of genetic epidemiological data about cardiovascular, neuropsychiatric and environment-related diseases there. By the end of 2006, PopGen had at its disposal samples from more than 45,000 volunteers to the project including control cohorts, as well as the accompanying clinical data from more than 3,500 patients.

### *oragen*

The Helmholtz research centre GSF has built up a collection on population-based health research in epidemiology, health economics and health services research.

This collection has helped with the analysis of a broad range of scientific, particularly epidemiological as well as population-genetic issues (cardiovascular diseases, obesity, diabetes, allergies, asthma, neurological diseases and cancers). In addition to extensive medical examinations, sociodemographic factors, lifestyle and dietary habits, family history, psychosocial information, recourse to medical services and the participant's own assessment of their state of health are also recorded. Plasma and serum samples from more than 18,000 test persons are in storage in nitrogen tanks, likewise the DNA of more than 18,000 test persons is available.

### *Blood donor biobank*

The »Blood Donor Biobank« was initiated in 2003 by the Blood Donation Service of the Bavarian Red Cross (BSD/BRK) and launched publicly in the middle of 2006. The BSD/BRK has placed its archive of retain samples collected from blood donors over the last five years at the disposal of biopharmaceutical companies and researchers. Thus for the first time large numbers of samples from a great many sick people are available from the time before their medical diagnosis. The BSD/BRK sample archive currently holds more than 3m plasma samples. Since the end of 2006, after obtaining consent, the samples and data from 5,000 blood donors who have been taken ill and where this is known are being recorded in the biobank. Severe and common diseases such as diabetes, cardiovascular diseases and cancer are in the foreground. If the research proves successful, 100,000 healthy blood donors will be prospectively registered in the biobank and accompanied medically for years to come. The biobank archive will then comprise far more than 1m plasma samples and therefore will also be one of the largest biobanks internationally.

### *Pharmaceutical industry*

Pharmaceutical companies which set up or operate biobanks are predominantly organised in the so-called Pharmacogenetics Working Group. It can be assumed that the following international pharmaceutical companies at least either operate or are currently establishing their own (larger) biobanks: Abbott Laboratories, AstraZeneca PLC, Bayer Schering Pharma AG, Bristol-Meyers Squibb Co., GlaxoSmithKline Ltd., Eli Lilly & Co., Merck & Co., Merck KGaA, Novartis GmbH, Pfizer Inc., Roche AG, and Wyeth Pharmaceutical. The expectations of the pharmaceutical industry for the future benefits of biobanks are concentrated on improving the knowledge of the molecular basis of diseases; on a better causal understanding of the disposition of diseases and the reactions of patient collectives to an active substance; developing safer and more effective medical



therapies; and identifying targets for the implementation of new medical treatments for previously hardly treatable or untreatable diseases.

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## BIOBANKS IN THE CONTEXT OF NATIONAL STRATEGIES

Biobanks are being established in a number of countries with in part completely different preconditions and intentions, scientific objectives or policy goals. National strategies could well play an important role, particularly if major public and social expectations are associated with the establishment and operation of biobanks. The report will examine three examples: The biobanks in Estonia, Iceland and Great Britain have not only attracted international attention because of their size, but rather also due to the concrete national economic and socio-political targets associated with them.

### *The national biobank in estonia*

The idea to establish a national database for the whole population, which would comprise not only genetic, clinical, and genealogical but also lifestyle data, was introduced into the public discussion at the end of 1998 by an association of Estonian scientists. The registration of three-quarters of the population, i.e. of approximately one million people was planned. In 2001 the Estonian parliament passed the Human Genes Research Act, which regulates questions relating to ownership and access among other things. A state foundation, the Estonian Genome Project Foundation was designated as administrator of the biobank and database in 2001. Around 10,000 samples were collected by the end of 2004, since then collection of data has stagnated. The samples and data collection should reach 100,000 samples by 2010 and new research projects have started. The original target of 1m was lowered, although 100,000 records from a population of 1.3m can still be regarded as representative.

At the same time as the decision was made at the end of 2001 to fund a biobank project for the whole population, the Estonian parliament also adopted a »research and development strategy« for the period from 2002 to 2006. The model of a »knowledge-based society« referred to the building up and consolidation of research as the key to the economic development of the country. However the preconditions for the implementation of this strategy remain modest. It is true that biomedical research is promoted on three levels (structural improvement of the infrastructure, co-operation between industry and research, disease research); nevertheless the biotechnology sector in Estonia is not particularly remarkable. An additional problem with the Estonian promotion of trade and



industry in a biomedical context is the lack of a suitable market for research and health care services. There are consequently no positive effects for the domestic economy.

The anticipated magnetic effect of the Estonian biobank project on major pharmaceutical corporations failed to materialise, and the economic prospects which the Estonian government associated with their support of the project did not come to pass. As the EGP has to do with pure research, anticipated effects on public health care cannot be expected for the time being either.

The government nonetheless wants to continue funding the biobank project in the future, as it is not only a national prestige project, but also a resource for research projects designed and co-ordinated in other EU countries, and thereby a means of integrating Estonia into the EU research area, which could provide positive feedback for the Estonian economy in the medium term.

#### *The national biobank in Iceland*

Iceland was the first country to plan a biobank designed to register the entire population. Right from the start its long existing genealogical database was unique worldwide. The information reaches back in part for more than 1,000 years. This wealth of genealogical knowledge makes the Icelandic population especially attractive for genetic studies.

In 1998, parliament passed an Act enabling the establishment of a health sector database providing for the extensive and general collection of medical and personal data for the whole population. The health data is gathered by hospitals and practising doctors throughout the country and transferred to a central database. In addition, the Act allows for the exclusive use of the database by the US company deCODE genetics in co-operation with its Icelandic subsidiary Islensk erfðagreining as licensee for twelve years. What is more the Act authorises deCODE to link the database to two further collections of data – the genetic and the genealogical (phylogenetic) data of the Icelandic population. By the end of 2002 deCODE had collected disease-related genetic data from approximately 100,000 Icelanders out of a total population of 290,000 and linked this with health and genealogical data. Disagreements with the data protection authority concerning data encryption procedures in particular, as well as the ascertainment of the Act as unconstitutional have caused the biobank project to fail in its original intent.



The state's dream of using biomedicine, biotechnology and biobanks as catalysts for comprehensive socio-economic and health policy innovation has not worked out. Major criticism was recently levelled at the operation of such an extensive biobank or health sector database with a great depth of social intervention by the general public and the health sector. The marketing of the data was both in the spotlight and under fire – genes as the common heritage of the Icelanders – marketed exclusively by a commercial firm.

### *UK biobank*

The UK biobank is currently the largest project worldwide and is one of the prospective population-related biobanks. According to its original plans it should provide the infrastructure to investigate the interaction between genetic and environmental factors relating to the occurrence of illnesses in particular. The UK Biobank is essentially funded by the following three sponsors: the Wellcome Trust, the Medical Research Council (MRC) and the Department of Health. A total of about 88m euros have been provided for the recruitment and storage of the samples and data over the next few years.

A three-month data and sample recruitment phase began in the middle of 2006 with 3,800 test persons from Manchester. The subsequent peer review process was positive and the extensive recruitment and development of the biobank started at the end of 2006. Samples and data from 500,000 volunteers between the ages of 40 and 69 years are to be collected and evaluated by 2010 (individual genetic and medical information, blood and urine samples, behavioural data). There is a non-profit enterprise (UK Biobank Ltd.) at the centre, which organises the collection of the samples and the biobank as well as exploiting their commercial use. Costs are estimated at around 90m euros. Six centres are affiliated, each of which is organised as an independent organisation. The principal objective of the UK Biobank is research into widespread diseases of civilisation. Randomly selected test persons are asked to complete a detailed questionnaire for the purpose of gathering extensive medically relevant data. In addition a blood sample is taken, which is subjected to molecular genetic analysis and registration. The follow-up analyses take place over the ensuing 20 to 30 years, outpatient clinical and hospital records are linked together for this purpose. Solid funding is currently guaranteed for ten years.

The legal regulation of the use of the biobank is rarely discussed, and also no concrete efforts are being made towards drawing up a specific law. Any references made to legal regulations refer to the prevailing Data Protection Act. The information provided by the operators and the principal sponsors is in principle

comprehensive. Information on participation procedures, scientific records and peer reviews is downloadable from the Internet, the draft by the Ethics and Governance Framework was available for comment. Parliament has also discussed the project; NGOs such as GeneWatch and Genetic Alert, and also the Parliamentary Office of Science and Technology (POST) have prepared numerous questions and information for members of parliament.

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## SIGNIFICANCE FOR RESEARCH AND HEALTH POLICY

As a result of the heterogeneity of biobanks, comprehensive assessments of the previous and possible future scientific significance of biobanks can hardly be made. The focus of the TAB project and this report on the new, heavily »genetically oriented« type follows the scientific and research policy debate of recent years. The undertaking of a differentiated observation of all the other, »traditional« biobanks, which in many cases may well have major scientific significance for pure and applied medical research, and often also for clinical practice, should remain the subject of a separate study.

Within the »genetically oriented« biobanks, there is frequently a differentiation made between disease-related and population-related biobanks, whereas a dividing line cannot be clearly drawn. It is believed that the disease-related biobanks produce more clearly nameable scientific advances in perception, but that these are »thematically« limited, whereas the population-related biobanks offer a »greater«, but more unstable increase in knowledge. The scientific and research policy debate is primarily about the possible future significance of biobanks, and in particular the question of whether population-related biobanks have to be as large and whether the parameters recorded should be as broad in scope as possible, in order to deal with the (potentially) widest possible range of research issues (as was or is the case in Estonia, Iceland and Great Britain). As an alternative there is a discussion of whether the focus of population-related approaches should not also be on particular diseases with a reference to existing hypotheses (which is the strategy of the largest corresponding German biobank, PopGen).

The crux of the scientific debate is the question of what potential the approaches of genetic epidemiology have to offer to advances in perception, and ultimately for practical applications in medicine. On the whole it seems plausible that biobanks, through the linking of clinical data with information on genetic and non-genetic exposure, will help us to better understand how a large number of diseases spread. It certainly does not seem very plausible that practically useful



## SUMMARY

predictive genetic opportunities for testing will arise from the knowledge of genetic mutations of multifactorial diseases, which – each for itself or where necessary also in specific combinations – indicate a rather moderate risk of the development of disease. Disenchantment has been spreading throughout the circle of researchers and industry for a number of years also in terms of the potential and prospects of so-called »pharmacogenomics or pharmacogenetics«.

The greatest scientific and in the long run also medical significance might well be the possible advances in perception following a consideration of the mode of action of the various genetic mutations, or the biochemical, cellular and physiological processes they influence during health and illness. Better comprehension could also provide starting points in the long-term for better therapeutic strategies. The question to be asked therefore is which type of biobank is most suitable for this – ultimately rather »classical« – approach. Here there is plenty to be said against the prospective »universal biobanks« and much to be said for focussed yet extensive and well characterised biobanks. What seem unsuitable, as these are inefficient and expensive in the long run, are the collections of material established individually by single scientists on an issue to issue basis.

Alongside approaches in genetic epidemiology (with corresponding biobanks), in future projects in *molecular* epidemiology could be of growing (and possibly even greater) importance. Their approach is to identify and investigate so-called prognosis markers on human biomaterials which, if necessary are subject to measurable changes long before the outbreak of disease and already indicate this (as opposed to genetic markers, which in cases of multifactorial diseases simply indicate a – usually low – risk). These markers already play an important role in cancer research and prognosis.

The TAB report explicitly does not deal with the issue of increasing genetisation (of medicine and society), as biobanks do not in our opinion offer a coherent analysis perspective for this as a focus for examination. The question as to whether the linkage of ever more research promotion activities by the BMBF under the umbrella or label of genomics (e.g. in the NGFN) constitutes a scientifically meaningful and desirable strategy or not, cannot be answered on the basis of this project. To answer this would require clarification of the question of whether promising alternative approaches are impeded or insufficiently promoted by this.

Both the discussion of the potential scientific and medical benefit of genetic epidemiology, as well as the analysis of the scientific debate concerning the orientation of UK Biobank, point ultimately to one central question or demand

which can hardly be disputed: the demand for comprehensive scientific quality assurance as well as for the continuous evaluation of the promotion of biobanks in terms of research policy.

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## LEGAL ETHICAL AND POLICY ASPECTS

One question for politics and society is whether the basic conditions shaped by existing law are sufficient to ensure the protection and at the same time the appropriate use of what are extremely personal data stored in biobanks. The objective would have to be both not to endanger the protection of the donors' samples and data, while at the same time providing the opportunity for the optimal exploitation of these materials and data in terms of their 'ethically sound' use.

There is an abundance of activities, approaches to solutions and proposals for regulation to deal with these problems on a national and international level. The German legislature has not yet taken concrete action in this regard. There has been discussion however for some time concerning the necessity of regulating the use of genetic data in the working world, in research and at private insurance companies, which could also be of relevance for the operation of biobanks. However the recording of population scale genetic data and its use in research and pharmaceuticals have not so far been included in preliminary deliberations on a planned genetic diagnostics law (Genetic Test Act) - not even within the framework of the implementation of an EU directive on cell and tissue donations into national law.

With reference to the legal and ethical issues and problem areas mentioned, the prevailing conditions for the establishment and operation of biobanks for the German legal area will be described; the possibilities as well as advantages and disadvantages of the respective operating types and legal form will be explained; and the fundamental legal and ethical demands made on the operation and maintenance of biobanks will be specified.

### *Ownership, rights of use, consent*

Ownership of biomaterial samples in a medical context is not legally indisputable. A differentiation has to be made between those samples which fall into the context of pure treatment, and those which were gathered from the outset for the purpose of research. Questions arise such as what »ownership« actually is in a legal sense, and in particular, in what sense biomaterials of human origin can be property at all, or what consequences the transfer of ownership of a sample



to a biobank can have on the range of the rights of use of this sample. Moreover questions are raised in particular concerning the range and extent of a transfer of rights to use samples/data from the patients/test persons to the biobank. A fundamental differentiation needs to be made between a treatment context, in which collection of biomaterials takes place directly in order to benefit the patient him/herself, and a research context, in which samples are collected for general purposes and at most indirectly for the donor's benefit.

The prevailing constitutional conditions for research with personal data include the freedom of research and teaching on the researchers' side and the right to informational self-determination on the patients'/test persons side. The (possible) collision of these basic rights in the context of research projects can be resolved, after considering both rights, through a declaration of consent made following detailed information: Predictive information may possibly result from genetic studies, decisively changing the previous view of duties to disclose or rights to obtain information about a patient/test person. So that the storage and use of biomaterials may also take place in keeping with the law from a data protection point of view, consent has to be formulated in such a way, that the permanent security of the operation is guaranteed, particularly regarding the central issues of consent: informing the persons concerned, the voluntary nature of the test person's consent and their capability of understanding. The conditions for the use of samples and data must be stated for the patients/test persons as specifically as possible in the declaration of consent, starting with the purpose, covering the period of use through to a transfer to third parties. If uncertainties remain concerning individual issues at the time of consent, then this uncertainty must be disclosed, in order to give the patients/test persons the opportunity to decide whether to consent to this uncertainty. Graded consent with options is assessed differently by experts; however this has apparently proven itself to be a feasible method in practice.

#### *Data protection*

The handling of samples in biobanks always involves two components: the actual sample in its physical form (as the bearer of potential information and data) and the accompanying data. The established organisational, processing and data protection provisions of medical research relating to biobanks need to be extended and specifically adjusted from the viewpoint of data processing and also data protection, namely for the following reasons:

- > Information relating to people is present along with the sample and thereby potentially at least data, which has not been transcribed and cannot be precisely

- assessed with regard to its scientific use as well as data protection risk potential.
- > As a rule with biobanks, neither future use with regard to concrete research projects and methodical approaches, nor an exact determination of the people who will work with the sample in future, can be anticipated. It is precisely here that the complexity of the situation lies, a suitably informative education of test persons including consent for a future use with far reaching application.
  - > The administration of references to the sample requires additional data, which in turn needs to be verified, to make sure it doesn't allow inferences to be drawn in individual cases to a particular patient or, as the case may be, to a disease.
  - > the information content and along with it the risk potential in terms of data protection can only be exactly estimated in individual cases, dependent on the nature (information density) of a sample, the method of analysis and the availability of comparative data collections. The effort invested in security measures for maintaining the samples and storing analysis data needs to be adjusted accordingly.

Four central conclusions can be recorded with regard to the relevance of personal rights and data protection laws: Personal rights and data protection regulations have absolute priority over (transferred) rights of ownership and use. Samples may not be collected against the wishes of the test person. Samples are to be stored separately from personal data and may only be passed on to third parties if they are pseudonymised for data protection reasons. The test person can withdraw consent for use at any time and demand the destruction or return of the sample (in so far as these have not already been anonymised and thereby can no longer be traced to people). Aspects of a possible incapacity to give consent (e.g. through accident, disease, death) need to be taken into consideration here.

### *Confidentiality*

The legal and ethical assessment of the operation of biobanks focuses in particular on whether these really could bring specific and new types of threat to confidentiality or a risk of discrimination in their train, if for instance data drawn from genetic or protein studies were to be linked with other data, for example from genealogical or lifestyle data. A situation could then arise in a data pool that different data are combined to form a more or less comprehensive picture of an individual or a group, and the firewalls which otherwise exist between different types of data and their transfer to third parties could be partly bypassed.

The situation could also be problematic during the processing or use of data by third parties (e.g. employers, insurance companies, health insurance companies).



Access to (genetic) data from biobanks could also be of interest to the state as an additional third party. Thus for instance the operators of biobanks could be obliged to make personal data available for policing purposes through a court order or by law. Research institutes for example, can neither rule out this kind of state access nor guarantee absolute confidentiality in their handling of personal data.

### *Public interest orientation*

In the context of the handling of human biomaterials and data, is it often argued that these also represent a public good, the duty of preservation and protection of which lies with the state, resulting in corresponding objectives and tasks for the common good. »Benefit sharing« and »access sharing« are among the elements which can ensure a public interest orientation in the case of biobanks.

Persons who donate biomaterials do not generally participate, at least not economically, in the commercially usable procedures and insights incorporated in the materials or arising from them, and for the most part they do not directly profit in medical terms either. It is often stated that solid reasons argue against the individual participation by sample donors in the economic benefits gained through the exploitation of their bodily substances. One fundamental reason for this for instance would be that relevant research is mostly based on the analysis of a large number of samples from a great many donors. For most results the specific or distinct contribution made by one individual to a product, a medicine, a patent or a potential medical treatment is not demonstrable. What is unaffected by this is however the information of a donor/test person by the operator of a biobank of possible commercial intended applications of research results, which are based on individual biological or genetic material.

The correlate of »benefit sharing« is »access sharing«. The relevant group of people in this case includes firstly those persons who have contributed samples and information about their lifestyle as well as about their family history. In this respect it is considered necessary that these persons have cheap or free access to tests, treatment and medicines, which may result from research with their materials. Secondly, »access sharing« refers to science. What is meant here is the granting of general and non-exclusive access to the materials and data collected in the different biobanks. The focus here among other things is the goal of providing support in particular for the otherwise rather neglected areas of research, especially at public and non-profit-making sponsored biobanks, in which pharmaceutical companies only have a slight interest for example.



*Trusteeship*

With the instrument of trusteeship an entity is addressed to control the personal assignment of samples to (genetic) data and additional records. In addition trustees can take on additional tasks, e.g. so as to comply with transparency and accountability requirements, but also to promote public discussion, in which donors/test persons and the public are consulted on priorities for research and use, and regularly presented with reports concerning the commercial use or the results of research with samples and data from biobanks. There are various ideas relating to potential models and operating types. Trustees could be used as independent intermediary authorities for the organisation of biobanks. They can act as non-profit, private or state institutions and in certain types of co-operation, which in turn include representatives of different interest groups. The type of organisational form to be given precedence depends upon the individual case.

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**SUMMARY**

Because of their potential importance for the health and social welfare system, private prudential and care needs and the growing scarcity of financial resources on the part of governments, insurance systems and private individuals, biobanks find themselves caught between the conflicting priorities of the interests of scientific insights and a public interest orientation on the one hand and private interests on the other hand. Linked to this is a multitude of new or more or less (un)solved issues associated with the collection, storage, handling, and use of samples and data as well as the social integration of these processes.

At the same time biomedical research – and thus also the biobanks – along with its medical practical and economic findings or applications have gained a new and growing political significance in recent years. Alongside intensively discussed legal and ethical questions, it is primarily research, innovation and health policy prospects which have allowed the significance and utilisation of biomedical developments appear of particular relevance in a national and international context.

*Health policy significance*

The fact that biobanks play a scientifically important role as a central research instrument of genomics is indisputable. With regard to the potential practical medical and thereby health policy significance of biobanks, a differentiation needs to be made between the different types, whereby the value of »tradition-



al« biobanks and by tendency also the disease-related biobanks of the new »genetic« type have only a few doubts cast on them. As regards the major population-related biobanks – and here not only the international examples of the »universal type«, but also only recently founded disease-related projects such as PopGen – it must be noted that their medical importance is thus far not yet discernible and remains uncertain for the future also. In view of the level of public funding for genomics, and thereby also for the operation of biobanks, it is surely necessary to remain systematically forward-looking and to accompany relevant research programmes and projects by questioning what (positive) effects they then (could) have for practical medicine and on public health. One example would be the objective of the research approach currently under construction and named »Public Health Genetics«.

#### *Benefits and acceptance*

As it is expected of the population, that they donate samples and data, there is a need to investigate and discuss the risks and the benefits in their entirety, from consent through to organisation and control. In doing so the problems of legitimate economic interests do not need to be expounded as a matter of principle. In terms of an ongoing discussion however, the potential advantages and benefits for donors should also be included in the discussion. This applies for example to the communication of research results to donors. A legitimate interest such as this results firstly from the right of informational self-determination, i.e. being permitted to know for example which information from individual donors could be used in relation to their health or a particular disease. Normally a direct benefit like this would not arrive without many years of research and trials of the results of this research first taking place. The general provision of information to patients/test persons concerning intended commercial applications is essential; they must be given the opportunity of rejecting a commercial application based upon their bodily material should the occasion arise.

A further significant area is the complex of problems concerning the respective specific informed consent of the person concerned with regard to the exploitation of his/her samples and data. By today's estimate it is precisely these aspects which are insofar of essential importance as the benefits of biobanks, which are used for diagnostic, therapeutic, preventive and in particular research purposes, which have to be weighed up against the potential risks of causing damage, the violation of integrity, the invasion of privacy, stigmatisation or discrimination. With this in mind an appropriate approach towards biobanks makes sense simply in order to also really be able to do justice to the immanent chances and risks in practice, in particularly in view of the expectation of the improved healing of

diseases on the one hand, and on the other hand the possible threat to the personal rights of patients in particular or the discrimination of population groups.

In view of the opportunities and risks described, it seems sensible to develop realistic prospects for the use and the protection of samples/data at least on a national and EU level. The (few) impulses which are available, through the German National Ethics Council in particular, and the concepts which have been developed internationally, offer a few pointers as to how an optimum design of biobanks could look.

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## COURSES OF ACTION

Of considerable importance for all concerned appears to be a basic certainty of action in terms of the establishment and operation of biobanks as well as in the institutional dealings with them. Several general measures can be named referring to this, in particular:

- > the determination of requirements for the technical security and the quality of biobanks; the quality inspection of the establishment and operation of biobanks and the implementation of continuous monitoring (auditing, inspections);
- > the registration of all biobanks and proof of quality inspections in a central, publicly accessible biobank register (to be established);
- > the mandatory licensing or accreditation of biobanks;
- > the establishment and unconditional observation of confidentiality as well as the requirements of data protection.
- > In order to achieve the targets mentioned or to implement these measures, the establishment of a central regulatory institution (e.g. following the model practised in Great Britain) could be considered, if necessary also through the appointment of a »national biobank representative«.

As there is as yet no (generalised) contact point for patients or sample donors, which could provide this information or consultation on the use (or abuse) of samples/data, it would furthermore be for biobanks to think about a representative to protect test persons/patients, either through the establishment of a central counselling centre or as a local »ombudsmodel« in hospitals or (affiliated) biobanks.

The discussion as to whether and how, and where necessary, to what extent (new) legal possibilities and conditions need to be discovered and initiated for the establishment and operation of biobanks is largely just beginning. The ques-



tions that are still open are of fundamental concern to all biobanks in which data is collected and stored for specified or also as yet unspecified research purposes. The following aspects are of considerable importance here:

#### *Data protection*

In principle all blood and tissue samples, especially the samples for genetic analyses, are explosive in terms of data protection, and require precisely defined, documented and controlled handling.

Legal regulation is required, which determines to what extent the establishment of biobanks in Germany should be permitted and what legal requirements they must fulfil. The following are particularly relevant from a data protection point of view:

- > the mandatory specification of data protection guidelines,
- > a statutory *prohibition of unauthorised reverse pseudonymisation*,
- > the guarantee of data security for the pseudonymised database,
- > the development of suitable *disclosure protection*,
- > *an exemption from seizure* in criminal proceedings as well as a
- > *right of refusal to testify* for researchers.

#### *Patients' consent*

There is broad agreement both nationally and internationally that assent to the collection and storage of biomedical samples and data in the context of biobanks on the part of the test persons/patients can only be provided in the form of informed consent. How this is to be achieved in practice however has not as yet been fully clarified. It appears that a one-off declaration of consent, signed when samples and data are registered or a biobank is established, does not suffice in all cases according to prevailing data protection criteria in Germany concerning the freedom of decision-making and discretion on the part of the persons concerned.

#### *Confidentiality of research*

What is more, a general requirement of *confidentiality of research* would be desirable in the opinion of the National Ethics Council and the Federal Commissioner for Data Protection precisely in the field of biomedical research. This would mean that the interests of the persons concerned could be better protected, as researchers in this case would be subject to a specific duty under criminal law

to maintain confidentiality with reference to personal data and the disclosure of personal data to third parties (e.g. authorities) would be legally prohibited. At the same time a requirement of confidentiality of research could also extend researchers' opportunities to process sensitive data securely.

### *Biobank law*

The essential aspects and problems of the use of biobanks for human medical research and application could, if necessary, be regulated within the framework of a »*national biobank law*«, which would in particular make legal provisions, pertaining to the definition and demarcation of biobanks among other things; codes of practice in cases of insolvency; regulations of jurisdiction for ethics commissions; the use of samples acquired through in the context of treatment for research purposes; and more.

### *Future prospects*

In the overall picture it becomes apparent that the use of human biomaterials (for research purposes) in the context of biobanks is not unproblematic. In practice the corresponding legal issues have to some extent only partly been realised, and it is expected in this respect that the relevant jurisprudential and legal ethical discussion of the use of human biomaterials will in future also be addressed in further detail and more intensively.

The essential objectives of the courses of action mentioned as examples would serve above all to strengthen the protection of the personal rights of test persons and patients who provide samples, data and additional information to biobanks. In addition the potential of the research and industrial sector of biobanks could be exploited in a controlled, quality assured and economically beneficial way, including ultimately also strengthening Germany as a research location in this field. An acceptable balance should be struck while doing so in order to avoid both over-regulation as well as rank growth.



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