Deutscher Ethikrat

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1 HUMAN BIOBANKS: SURVEY AND DEVELOPMENTS

1.1 Introduction

The term human biobanks usually refers to collections of samples of human body substances (e.g. tissue, blood, DNA) which are linked to personal data and socio-demographic information about the donors of the material. They have a dual nature as collections of samples and data.[1] Most currently existing biobanks are research biobanks, that is, systems which collect samples and data of human origin and either use these for their own research or make them available to third parties for research purposes. They play a central role in research on the causes and mechanisms of a large number of illnesses and their treatment. There are also biobanks containing material which is used for diagnostic and therapeutical purposes. Classic examples of this are pathology departments, blood donor services or umbilical cord blood banks.

The subject of this Opinion is human biobanks for scientific research (referred to below as biobanks). These are collections of human biological material which is linked to health-related and other information about the donors. Their purpose is the use of the collection for scientific research. They are designed to be used for a variety of research purposes, some of which will only be apparent in the future.[2]

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1 German National Ethics Council (ed.): Biobanks for research. Opinion. Berlin: 2004, 9. Also available online: http://www.ethikrat.org/files/ner_opinion_biobanks.pdf [2010-05-27].

2 Biobanks which store human biological material such as umbilical cord blood for therapeutic purposes are not the subject of this Opinion. In Europe, they are governed by Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells (known as the Tissue Directive, OJEU L 102, 48) and in Germany by the *Gesetz über Qualität und Sicherheit von menschlichen Geweben und Zellen* (Act on Quality and Safety of Human Tissues and Cells, also known as Human Tissue Act, BGBl. I 2007, 1574), which

Biobanks raise ethical and legal questions which extend from the protection of individual rights to the global governance of research infrastructures. The *Gesetz über genetische Untersuchungen bei Menschen* (Human Genetic Examination Act, also known as Genetic Diagnosis Act), which entered into force in February 2010, contains no provisions on these questions. Section 2(2) provides that the Act does not apply, amongst other things, to genetic examinations and analyses that are undertaken for research purposes. As a result, there are at present no specific statutory provisions for biobanks in Germany.

Both the former German National Ethics Council[3] and the Study Commission[4] of the *Bundestag* (German Federal Parliament) have considered biobanks in earlier opinions and have formulated recommendations on dealing with samples and data of human origin which contain starting points for possible legislation on biobanks. Since that time, however, there has been more dynamic development in this area. Not only are new biobanks constantly being established, but they are used in new forms and dimensions, which makes it necessary to consider the subject again. However, the current developments do not require a completely new assessment, and consequently the German Ethics Council is able to refer to the above publications in the present Opinion.

The current developments with regard to establishing biobanks and biobank research can be summarized as follows:[5]

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implemented the Tissue Directive in German law, and by the amendments to the *Transplantationsgesetz* (Transplantation Act) and the *Arzneimittelgesetz* (Medicinal Products Act) made by the latter.

3 German National Ethics Council 2004 (cf. fn. 1).

4 In its final report on the topic "Genetic data", the Study Commission on Law and Ethics of Modern Medicine considered research biobanks. See *Deutscher Bundestag* (ed.): *Enquete-Kommission Recht und Ethik der modernen Medizin. Schlussbericht*. Berlin: 2002, 324-328. Also available online: http://dip21.bundestag.de/dip21/btd/14/090/1409020.pdf [2010-05-27], 150-152.

5 Kollek, R.: *Biobanken – medizinischer Fortschritt und datenschutzrechtliche Probleme. Vorgänge* 47, 184 (2008), 59-69.

1.2 Quantitative expansion

The number of known biobanks and of the activities in connection with them is increasing both nationally and internationally. Although biobank registers which reliably document the quantitative development of biobanks are at present only in the process of being set up, the references to human biobanks in specialized literature is growing by leaps and bounds, and this indicates a strong expansion: the number of scientific articles referring to human biobanks has increased fivefold since 2004.[6] Individual biobanks are being established for a large number of research projects which deal with the identification of genetic risk factors or questions of genetic epidemiology. One of the recent developments is the *Helmholtz-Kohorte* (Helmholtz Cohort)[7], a large-scale population study which is designed to research common chronic illnesses such as diabetes, cancer, cardiovascular diseases and dementia and is to contain samples from 200,000 persons.

This means that the project is on the same scale as national biobanks such as those that have been in development for some time in the United Kingdom, Norway, Sweden and other countries. The UK Biobank, designed to cover 500,000 persons, at present already contains samples and data of over 450,000 persons.[8] The Norwegian biobank Biohealth Norway is also to cover 500,000 persons, which is one-tenth of the total population.[9] The Swedish national biobank programme already contains between 50 and 100 million samples; it increases by three

6 PubMed search carried out by the *Telematikplattform für medizinische Forschungsnetze* (TMF) , personal information from Roman Siddiqui, TMF.

7 Cf. press release of the Helmholtz Centre for Infection Research of 13 November 2008. Online: http://www.helmholtz-hzi.de/de/presse_und_oeffentlichkeit/pressemitteilungen/ansicht/article/complete/neuer_round_table_fuer_forschung_und_gesundheitspolitik [2010-05-27].

8 Figure for 3 May 2010: 459 120 persons. Cf. http://www.ukbiobank.ac.uk [2010-05-03].

9 Cf. http://www.fhi.no/eway/default.aspx?pid=238&trg=MainArea_5811&MainArea_5811=5906:0:15,4627:1:0:0:::0:0 [2010-05-03].

to four million samples every year.[10] These examples illustrate the growing importance of biobanks, and at present no end of this development is in sight.

1.3 Increase of information included

The files linked to samples in biobanks contain the clinical data of a patient or donor (blood test results, diagnoses of illnesses, results of imaging techniques etc.), and also an increasing amount of socio-demographic data, genetic data and information on lifestyle. The information contained in them is constantly increasing as a result of repeated collection of data and scientific analysis, some of whose results are entered in the files. The information content of human biological material is potentially inexhaustible.

As a result of the increase in information stored, the records are also becoming increasingly more individualized; ultimately, there is only one person with a particular combination of characteristics. This has far-reaching consequences for anonymizing or pseudonymizing the records (see 1.4 and 2.4).

1.4 Growing re-identifiability

As a rule, the sample-related data are pseudonymized (aliased) and in this form they are stored or transferred to other researchers. "'Aliasing' shall mean replacing the data subject's name and other identifying features with another identifier in order to make it impossible or extremely difficult to identify the data subject."[11] The connection between pseudonymized data and identifying data of the donor (name, address, telephone

10 Repeat samples from individual persons are taken and stored. Cf. http://www.biobanks.se [2010-05-03].

11 Section 3(6a) of the *Bundesdatenschutzgesetz* (Federal Data Protection Act).

number etc.) may only be made by authorized persons who are bound to secrecy.

Anonymizing means that personal data are changed in such a way "that information concerning personal or material circumstances cannot be attributed to an identified or identifiable natural person or that such attribution would require a disproportionate amount of time, expense and effort."[12] In addition, the code which is capable of creating a connection between samples and data on the one hand and the donor on the other hand is irreversibly deleted.

However, the more individual data a record contains, the harder it is to pseudonymize or anonymize it, since the greater is the totality of individual data recorded, the more likely it becomes that it can only apply to one specific individual. Genetic analyses aggravate this problem, since they often create an individual, unmistakable genetic pattern or "profile" of a person.[13] If identifiable reference material is available elsewhere, the donor could be identified despite pseudonymization or anonymization of the record or the sample.

1.5 Networking

It is necessary to examine a large number of persons in order to discover small effects of individual factors which influence health, but individual biobanks often do not have the required number of well characterized donor materials. One solution to this problem is networking a number of biobanks, merging

12 Section 3(6) of the Federal Data Protection Act.

13 Cf. also Greely, H. T.: The uneasy ethical and legal underpinnings of large-scale genomic biobanks. Annual Review of Genomics and Human Genetics 8 (2007), 343-64; Heeney, C. et al.: Assessing the Privacy Risks of Data Sharing in Genomics. Public Health Genomics (online), of 29 March 2010; Karp, D. R. et al.: Ethical and practical issues associated with aggregating databases. PLoS Medicine 5, 9 (2008), e190; Malin, B.: Re-identification of familial database records. AMIA Annual Symposium Proceedings (2006), 524-528; Malin, B.; Sweeney, L.: Re-identification of DNA through an automated linkage process. AMIA Annual Symposium Proceedings (2001), 423-427.

their records and evaluating them collectively. This gives access to larger cohorts than would be possible through individual biobanks.

In Germany, the Federal Ministry of Education and Research, for example, strongly urges that these ideas should be implemented in practice. This includes the development of concepts for networking biobanks and for increasing the efficiency of their use. One example of this kind is being tested and engineered as part of the Central Research Infrastructure for molecular Pathology (CRIP).[14] Using this infrastructure, information on human tissue samples and data which are stored in the affiliated pathology departments in Germany and Austria are made available to enable research projects to be initiated over the internet. Another example of networking exists between selected biobanks which belong to the National Genome Research Network. The following have been integrated: the biobanks of the Competence Networks Paediatric Oncology and Haematology, Dementia, Heart Failure, Sepsis, Parkinson's Disease and HIV/AIDS. Here, as in the case of CRIP, a central contact point was established to request biological materials, which are transferred to the relevant network in response to project applications from external partners. Taken together, these models are seen as preliminary stages in the integration of German biobanks in European research networks (see 1.6).[15]

1.6 Internationalization

The trend towards networking can also be seen internationally. In March 2008, for example, as part of a project of the European Strategy Forum on Research Infrastructures sponsored by the EU Commission, the European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) was established. It

14 For details, see http://www.crip.fraunhofer.de/de/site_overview [2010-04-23].
15 Cf. http://www.bbmri.de [2010-05-03].

is intended to comprise approximately 100 biobanks from all over Europe.[16] It is the aim of this initiative to create an organizational infrastructure for the pan-European networking of biobanks and to enable the cross-border exchange of samples and data for research; at present, the legal aspects of this have not yet been sufficiently clarified.

There are also discussions on multi-national associations of biobanks extending outside Europe. In such cases, the data would leave the European Union legal area and their use would no longer be governed by EU data protection law. At present there are no internationally binding provisions or treaties either inside or outside the EU on the transfer of research samples as such and their handling.

1.7 Privatization and commercialization

Research biobanks are mainly, but certainly not only, operated by public agencies. For example, a large number of national and international pharmaceutical companies establish biobanks in connection with clinical studies. These samples are not only used for their own research, but are sometimes also sold to third parties. Such sales are part of the business model of some companies which develop and operate biobanks.[17]

Other companies offer biomedical or genetic services, such as examinations for predispositions to illnesses or genetic drug intolerances. In addition, some of them also carry out research using the samples and data supplied to them, for example in order to improve their own products and services. In this connection, they may also grant partner enterprises access to personal information of the customers.[18]

16 Cf. http://www.bbmri.eu [2010-05-03].
17 Cf. *inter alia* http://www.indivumed.com [2010-05-04].
18 Examples of this group of companies are 23andMe from the USA (www.23andme.com), deCODEme from Iceland (www.decodeme.com) and Navigenics from California (www.navigenics.com).

1.8 Extension of purposes and third-party access

Until quite recently, tissue collections were used primarily in fundamental biological and medical research. In the course of genome research and the development of individualized medicine, such collections have become increasingly of interest to applied research too, such as drug development. In genetic epidemiology, such collections of samples are used to an increasing extent in order to establish the distribution of genetic susceptibilities to illness and different populations and to develop health policy strategies on this basis.

Not only the research institutions which have established biobanks, but also third parties may be interested in using biobanks. This applies, for example, to insurance companies and employers, but also to state agencies, for example in connection with warding off danger and criminal prosecution and to identify victims of catastrophes or to establish identity in connection with litigation in the civil courts. Such a use of biobanks has already occurred in Sweden.[19] There are discussions at present as to whether the Swedish Biobank Act should be amended and the possibilities of access for criminal investigations by the police should be extended.[20] In Germany too, it is in principle possible for the security services to access biobank samples and data. It may be assumed that the interest of private and state agencies in using systematically designed and informative biobanks will increase. Such access raises central questions as to rights of personality and data protection.

19 For example, the nationwide PKU biobank, which since 1975 has collected DNA from every neonate in order to research the metabolic disease phenylketonuria (PKU), was used in 2003 in order to convict the murderer of the Swedish foreign minister Anna Lindh, and later to identify victims of the December 2004 tsunami.

20 Swedish *Kommittédirektiv* 2008:71. Online: http://www.sou.gov.se/kommittedirektiv/2008/dir2008_71.pdf [2010-05-03].

2 PROTECTION OF FUNDAMENTAL RIGHTS: BACKGROUND AND NEW CHALLENGES

2.1 Introduction

In principle, biobanks are subject to the same precept as research on human beings in general: the fundamental rights of the persons affected are enshrined in the *Grundgesetz* (Basic Law) and must be respected; their dignity and their right to life and physical integrity must be respected just like their right of personality and their right to informational self-determination.

The constitutionally guaranteed freedom of research does not remove the obligation to observe these fundamental rights. Consequently, encroachments upon bodily integrity – provided they are not authorized by statute – require the express consent of the persons affected. This consent must be preceded by appropriate information on the purpose, significance and implications of the encroachment (informed consent). If, therefore, blood or tissue samples are taken from a person for the specific purpose of research and/or storage in a biobank, the donor must give his[21] informed consent. The same applies to the collection and processing of personal data for research purposes: without the informed consent of the persons affected, this is unlawful, except where statute provides otherwise.

In connection with research on material which has already been separated from the body, where, for example, it was taken for the purpose of diagnosis and therapy, but later is to be used for research, there is no question that human dignity is sacrosanct; the guarantee of dignity only comes into consideration here as a reinforcement of other aspects of fundamental rights, such as the general right of personality and the right of

21 For convenience, the masculine form is used where applicable for both sexes throughout this translation [translator's note].

informational self-determination. None of the constitutional guarantees of protection which apply to the donor are absolute; instead, they are subject to the rule that legal interests must be weighed against each other. With specific regard to the requirement of informed consent to the use of biomaterials and biological data, therefore, the high priority of freedom of research must be taken into account when interests are weighed in this way. The data protection Acts of the Federal Government and the Federal *Länder* make it possible to give priority to scientific research in a weighing of legal interests even where particularly sensitive and therefore specially protected data, such as information on health or on sex life, are to be processed. Although the provisions are sometimes inconsistent (see 2.2), it is the fundamental requirement for the use of data that the scientific interest must outweigh the interests of the persons affected, and that the research purpose can be achieved only in this way, or alternatively only with disproportionate expense and effort. This weighing of interests may also be applied with regard to the use of bodily materials.[22]

It is therefore plain to see that concessions are readily made to the informational expectations of scientific research. However, as set out above, biobank research does have a number of special features which are either not taken account of or inadequately taken account of in present legislation on clinical and medical research or on data protection. As a result, there is a lack of provisions for biobanks which take account of these special features. Below, we outline how urgently such provisions are needed.

22 German National Ethics Council 2004, 44 ff. (cf. fn. 1).

2.2 Purpose-restricted use of data

The basis for biobank research as elsewhere is that personal data[23] may be collected and used only for a purpose specified in advance.[24]

However, the data protection Acts of the Federal Government and the *Länder* and the hospital or health data protection Acts and secondary legislation, some of which are *Länder* legislation, contain extremely diverse provisions as to how far deviation from this principle is permitted. There are no specific provisions relating to the special structural features of biobanks with regard to limitation of use to specific purposes. There are differing provisions for scientific research in public and private agencies, a distinction which is unconvincing, in particular with regard to biobanks. In some *Länder*, the affected person's consent may be dispensed with only for research carried out by the relevant hospital itself. In other *Länder*, the use of personal data without the affected person's consent is permitted more widely and includes scientific research outside the relevant hospital. The legal requirements therefore vary widely. Some legislation attaches weight to ensuring that concerns of the affected person which merit protection are not adversely affected. Other legislation, on the other hand, also permits data to be used for research purposes if public interest in carrying out the research project outweighs or substantially outweighs the concerns of the affected person which merit protection; in some cases, it is also required that the research purpose can otherwise either not be achieved or be achieved only with disproportionate expense and effort. Some data protection Acts

23 In contrast to anonymized data, pseudonymized data are also personal, since the connection to the person still exists.

24 By way of example, section 4(1) of the Federal Data Protection Act: "The collection, processing and use of personal data shall be lawful only if permitted or ordered by this Act or other law, or if the data subject has provided consent."; section 4a(1): "Consent shall be effective only when based on the data subject's free decision. Data subjects shall be informed of the purpose of collection, processing or use and, as necessary in the individual case or on request, of the consequences of withholding consent."

refer indiscriminately to "research", while others permit data processing only "for a specific research project". Some legislation additionally requires data protection officers or authorizing agencies to be involved.

A question connected to the principle of limitation of use to specific purposes is how specifically the donor's consent must relate to the later use of the sample and data material. This question too is not answered by the data privacy Acts with sufficient clarity. For example, the views of data protection officers and ethics commissions on this aspect vary widely. Some require that the donor knows the specific research project for which his sample and data material is to be used. Others hold it sufficient if the donor is informed of the research field (e.g. cancer research, dementia research). Others still are satisfied with an even broader consent ("medical research"). On the one hand it is pointed out that the donor cannot give *informed* consent if he does not know exactly what he is consenting to. The purpose "medical research", it is argued, is also not precise enough to show the donor the scope of his consent. This is countered by the argument that it is part of a person's right of self-determination, when he is aware that a situation is uncertain, to be able to accept this very uncertainty. Consequently, the argument continues, it is only necessary for the donor to be informed that the concrete future use is uncertain and to agree to accept this situation. The requirement of a more narrowly expressed consent would call into question the biobank principle as the infrastructure for research purposes which are as yet indefinite.

2.3 Useful life of research materials and data

The limitation of use to specific purposes laid down in data protection law has the consequence that the data collected for a specific purpose can only ever be used for a limited period of time defined by the achievement of the purpose. This means

that the aim of processing determines not only the particulars of use, but also its duration. The principle of *time limitation* of the use of samples and data is thus one of the fundamental pillars on which the present concept of data protection is founded.

Admittedly, the permissible duration of the use of samples and data is itself the subject of disagreement as to how far consent reaches: the more narrowly the consent is worded, the more likely this is to imply a time limitation of the use of samples and data.

In addition, there is the following problem: when the purpose of the relevant collection of data is satisfied, it is in principle necessary to destroy the data. However, in relation to biobanks as an import research resource, this requirement is more problematic, in three respects, the more narrowly the purpose is defined:

Firstly, the material used in each case is not superfluous for the mere reason that it has been processed for a project which has now been completed; against the background of scientific research which is not oriented towards or perceived in relation to merely individual projects, on the contrary, it remains a source of information which is fundamentally of unchanged importance.

Secondly, reflections on the original project, and a fortiori a critical review of it, presuppose that the material specifically used is still accessible. Both these aspects therefore support the need that the materials and the data collected from them should continue to be stored.

Thirdly, after the completion of such examinations, new research suggestions may arise which can be pursued only with the use of the materials already acquired and the data collected from them. From this aspect too it may be desirable not to limit the use of samples and data to one research project or to a specified period of time.

Networked systems, for reasons of quality assurance and data security, already contain a large number of backup copies,

and consequently it is scarcely possible to guarantee that the data will be completely deleted. This also applies in the case where a donor later revokes his consent to the use of his samples and data.[25]

When personal data, once collected, may potentially be available with no time limitation, this presents enormous challenges for their legal and technical protection. If the present requirements governing the processing of personal data are to be relaxed for scientific research purposes, this will be all the easier the more it is compensated for by making the data absolutely inaccessible for non-scientific purposes, that is, if there is a binding requirement that the use of data is to be reserved for scientific research, for the period of time researchers regard as necessary in each case.

2.4 Anonymization and re-identification

Restrictions on use for data protection relate to the processing of personal information. If the connection to a person is removed by anonymization, then by definition the data are no longer personal data; their use is therefore not subject to the restrictions of data protection law. But anonymized data are always open to the risk of re-identification. Samples and records containing genetic data aggravate this problem (see 1.4).

The question arising here is whether the growing danger of re-identification can be neutralized by means which are directly connected with the function and the organization of biobanks. Here too, the context and aim of the use of the data are convenient starting points. If scientific research could be established as the condition for use, the effects of a possible

25 Thus, for example, the UK Biobank informs donors that, although data from participants can be made unusable, it is not possible to destroy it completely. This, it states, is due to the development of complex IT systems designed to protect the integrity and security of those people who have taken part. Cf. http://www.ukbiobank.ac.uk/docs/Nofurtheruse.pdf [2010-05-03].

re-identification could be assessed; they would be restricted to the domain of science.[26] If a ban on access were laid down in favour of scientific research, the decisive factor here might be how reliably such a ban on access could prevent non-scientific use.

2.5 Providing donors with information

Although it is natural to seek provisions for dealing with samples and data in biobanks which fit in well with the particular conditions of the scientific research process, the concerns of the persons affected must certainly not be overlooked in doing so. Clear limits of use do guarantee a certain protection of those affected, but they are not sufficient to completely preserve their rights and interests. The processing of their data, which from a scientific point of view is necessary, must therefore be combined with provision of information which is tailored to the persons affected and which clearly states the special features of biobanks and their use.

The donors disclose information without being fully aware at the date when they do so of how their samples and data will later be used. This calls for a high degree of trust between donor and biobank. To guarantee this trust, the procedure itself, the provisions governing it and the activities of the biobank must be transparent. Depending on the degree to which this transparency is guaranteed by law, it may be expected that donors are readier to cooperate and possibly also to accept a more extended use of samples and data. The donors would then have the possibility at all times to obtain information on the activities of the biobank and the whereabouts of their samples and data.

There are shortcomings in the provision of information, which are tolerated by the data protection Acts. Not least in

26 On the distinction between scientific research and other areas, see Chapter 3.

view of these shortcomings it is important that the constantly expanding possibilities of research should be accompanied by the highest degree of transparency of the activities of biobanks and by an ongoing duty of documentation. Only then could the persons affected reliably follow what happens to their data; in addition, they would then be in the position to effectively exercise their rights guaranteed in the data protection Acts (e.g. in the form of revoking the right of use).

The informing and consent of donors must therefore be structured in such a way that the essential purposes and processes of collection and processing of personal samples and data are disclosed as part of biobank research, and the donor knows what he is agreeing to when he provides his samples and data for biobank purposes. In addition, however, it appears necessary to provide supporting measures which create trust and transparency, since in view of the nature of biobank research the donors necessarily have a lack of information which needs to be compensated for.

2.6 Conclusions

The establishment of biobanks makes it necessary for the present provisions on the protection of the general right of personality of the donors to be adapted to the new situation. The recently passed Genetic Diagnosis Act did not react to this need for legislation.[27]

In view of the challenges set out above and the possible implications for the individual and society, the German Ethics Council finds that specific legislation is necessary for biobanks or for biobank research.

27 See 1.1.

3 "BIOBANK" AS THE SUBJECT OF SPECIFIC LEGISLATION: DEFINITION AND DELIMITATION

It is no easy task to objectively define the collections of samples of human bodily material with associated data which are to be governed by a provision specifically for *biobanks*. This is because collections of samples and data of this kind differ widely in size and have varied aims and intended duration of storage. If one defines a biobank very broadly, it even includes a collection of a very small number of samples which are examined to answer a narrow question as part of a doctoral thesis and are deleted immediately after the question is answered. The question arises as to whether this should be subject to the same requirements as a national biobank with no time limitation containing hundreds of thousands of samples. Certainly, considerations of practicability and financing of research argue against such similar treatment, but at the same time it is scarcely convincing to make the application of a statutory provision for biobanks conditional solely on the number of samples collected, for the challenges for donor protection set out above are just the same, for example, where a number of small collections of material are internationally connected as they are for very large individual biobanks. In addition, subjective elements, for example the *planned* duration of use, have limited value as definition criteria, because intentions and plans may change rapidly.

An argument in favour of a broad definition of biobanks as the subject of statutory provisions is that a statute may certainly make distinctions in the legal consequences, that is, can react differently to the specific problems of different biobanks. The question as to whether a collection is or is not a biobank within the meaning of the statutory provision does not then determine whether particular biobanks remain completely unregulated.

Against this background, every collection should be the subject of the statutory provisions for biobanks proposed below if it satisfies the following three criteria:

a) It contains genetic material originating from humans with related data.
b) Its samples are electronically linked to personal information (possibly pseudonymized) and further information, in particular relating to health.
c) Its samples and data are collected, preserved or used for purposes of scientific research.

The three criteria set out here also cover collections which are narrowly defined in topic and duration and for which there are no plans for transfer to "other agencies" within the meaning of data protection law. This includes a large number of project-related collections which are established in connection with academic theses and dissertations.

However, such collections should not be subject to any unreasonable restrictions. Nevertheless, they should be given the privileges set out below, which protect the material and the related data from non-research-related access. In the following, for this reason, it will be set out in each case which requirements also apply to such project-based collections and which are only to apply to biobanks which are unrestricted in topic and duration.

If a collection which is narrowly defined in topic and duration is later transferred to one with no limitation of intended use and of duration, then the consent of the donors must be obtained and the extended statutory provisions must also be complied with.

The proposal set out below not only protects the concerns of the donors and their fundamental rights, but also guarantees the protection of the freedom of science and research guaranteed by Article 5(3) of the Basic Law. This includes "the processes, practices and decisions in the search for knowledge,

its interpretation and dissemination, which are based on science's own laws".[28] This applies irrespective of whether science is pursued academically at universities or in other forms of organization, for example in research institutions of commercial enterprises. Another aspect which is unimportant for the concept of scientific research is the distinction between general research and applied research; the decisive factor is that scientific standards are preserved in obtaining new scientific knowledge.[29]

The freedom of science and research applies not only to the activities themselves, but also to institutions which are indispensable to protect the constitutionally guaranteed sphere of freedom, because only through these institutions is free scientific activity possible.[30] Accordingly, the archives statutes of the Federal Government and the *Länder* contain an objectification of the particular value of specific data for research.[31] Section 40 of the Federal Data Protection Act is also orientated towards the structure and aims of the relevant institution, not towards the individual project.[32]

The restriction of the following proposal to research biobanks also means that collections which are established for police or forensic purposes are also excluded. Other collections excluded are collections whose purpose is to sell the samples and/or data contained in them; the special provisions proposed below do not apply to them. In the case of such collections, therefore, the existing general statutory provisions apply.

Finally, the same applies to collections which are established or maintained exclusively for therapeutical purposes

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28 Cf. BVerfGE 35, 79 (112); 47, 327 (367); 90, 1 (11 f.); 111, 333 (354); 122, 89 (105) [unofficial translation].

29 Krüger, H.: *Forschung*. In: Flämig, C.; Kimminich, O.; Krüger, H. (ed.): *Handbuch des Wissenschaftsrechts*. Berlin: 1996, 261 (262 f.).

30 BVerfG, NVwZ 2003, 600; cf. also BVerfGE 85, 360 (384 f.).

31 Cf. section 5(3) of the *Bundesarchivgesetz* (Federal Archives Act).

32 Simitis, S. (ed.): *Bundesdatenschutzgesetz* [Commentary]. Baden-Baden: 2006, Sec. 40 para. 35 ff. (38).

(e.g. umbilical cord blood banks) or diagnostic purposes (e.g. tissue sections or samples for pathological examinations).[33] The boundary between diagnosis, therapy and research may occasionally be hard to draw, but this problem exists in other contexts too, without the demarcation having been called into question as such. This can be seen, for example, when a decision has to be made as to whether a medicinal product is to be used, in accordance with standard medical practice, as part of an attempt to cure an individual, or as part of a clinical trial within the meaning of section 40 ff. of the Medicinal Products Act. Here too, the demarcation is to be based on whether increase of knowledge – in this case beyond the individual case – is in the foreground.

Where a collection of samples and data serves more than one purpose, the highest potential level of donor protection should apply.

33 As soon as such collections are also used for research purposes, in each case the provisions drafted for human biobanks that are project-related or not restricted in topic and duration apply.

4 PROPOSAL FOR A LEGISLATIVE CONCEPT

4.1 Introduction

Previous concepts on the protection of donors' interests have been essentially based – parallel to traditional clinical research – on the donors' informed consent. However, biobanks have special structural features, and consequently an individual's consent can give only limited protection, since it is given against the background of limited information. The concept of consent should therefore be supplemented by institutional and procedural rules which both set objective limits and also permit flexibility for research with biobanks. This is likely to increase acceptance on the part of the donors and remove previous objections on grounds of data protection.

4.2 The five-pillar concept

The German Ethics Council proposes a five-pillar concept for biobank legislation. The five pillars of this concept are the following:

1. the introduction of biobank secrecy,
2. the definition of permissible use,
3. the involvement of ethics commissions,
4. quality assurance in connection with data protection,
5. transparency of the aims and procedures of a biobank.

Whereas biobank secrecy should apply for all biobanks, the structuring of the other four pillars may take account of the varying requirements of different types of biobank, in particular with regard to how specific the research purposes are.

4.2.1 Biobank secrecy

Biobanks are the interface where various players meet, each with their specific interests. Research needs samples and data in the form of large biobanks in order to follow up population-related projects. Longitudinal research designs and risk-group-specific analyses in particular require information that can be individualized for their purposes. Even if, in the individual case, a biobank may have a concretely defined purpose, biobanks always have the nature of a collection of material and data which may also be available for projects which have not yet been defined at the time when the material and data is collected. Persons who provide samples and data disclose information without being fully aware at the date when they do so of how their samples and data will later be used.

If one accepts biobanks as resources for scientific research, provisions are necessary to permit a less restrictive limitation of use to specific purposes for the use of biobank materials and data than is provided for in current data protection law. Above and beyond the project-related intended purpose, it must be permissible to relate the intended use to medical research as a whole. At the same time, the quantitative and qualitative changes in the field of biobank research call for a correspondingly increased, effective and long-term protection of donors' fundamental rights.

Introduction and safeguarding of biobank secrecy

The most promising way to satisfy this requirement of protection is a provision of biobank secrecy which safeguards the samples and data stored in biobanks or transferred elsewhere by their operators against all access which is not legitimized by the purpose of scientific research. If the limitation of use to a specific purpose is removed, this should be compensated for by general biobank secrecy legislation which guarantees protection against all the world of the samples and data stored in a biobank. This addresses both the relationship between

the donors and all persons who obtain access to samples and data on the basis of a research-related right of use and also the shielding of the samples and data stored in biobanks against third parties (e.g. insurance companies, employers, state agencies). In this way, biobank secrecy protects the rights of personality and the right of informational self-determination of the donors against private abuse and against government encroachments. This must apply to collections of every size and nature which satisfy the three criteria named in Chapter 3.

In its specific provisions, biobank secrecy must protect in more than one direction; there are models for this in current law, but as yet no specific provisions for biobanks:

a) Biobank secrecy must include a duty of professional discretion: It must be prohibited to transfer personal samples or data to persons and agencies outside the domain of science. The target group of this duty of confidentiality includes not only the operators and employees of the biobank, but also the researchers and their assistants who use the information. This could be achieved by extending the duty of professional discretion as laid down in section 203 of the *Strafgesetzbuch* (Criminal Code).
b) All persons who work with anonymized or pseudonymized samples or data must be prohibited from taking measures to identify the donor.
c) External agencies (e.g. insurance companies, employers) must be subjected to a prohibition of the use of personal information which is obtained with the use of biobank materials.
d) In addition, there must also be provisions defining the right to refuse to give evidence of persons with a duty of professional discretion (comparable to section 53 of the *Strafprozessordnung* [Code of Criminal Procedure]) which prevents these persons from having to testify as witnesses and thus break their duty of professional discretion to a state agency.

e) In addition, biobank secrecy must prohibit non-research persons and agencies from accessing information relating to individual samples which is accessible in the domain of science. This would be analogous to the prohibitions on seizure of section 97 of the Code of Criminal Procedure and above all corresponding to the restrictions on matching data within the meaning of electronic profile searching in section 98a of the Code of Criminal Procedure.

According to the case law of the Federal Constitutional Court, the right to informational self-determination supports and extends the protection of freedom of conduct and privacy in terms of fundamental rights

> "by already making it start at the level of endangerment of the personality. Such an endangerment situation can already arise in the run-up to concrete threats to specific legal interests, in particular if personal information can be used and linked in a manner which the person concerned can neither detect nor prevent. The extent of protection of the right to informational self-determination is not restricted here to information which is already sensitive by its nature and hence already protected by fundamental rights. Depending on the purpose of access and the existing processing and linking facilities, the use of personal data which per se has only little information content can also have an impact on the privacy and freedom of conduct of the person concerned in terms of fundamental rights […]. The endangerments of personality to be averted with the right to informational self-determination emerge from the manifold possibilities open to the state, and where appropriate also to private players […] to collect, process and use personal data. Such information may lead to the creation of further information, above all using electronic data processing, and to conclusions which may both impair the interests of the person concerned in confidentiality, which

are protected by fundamental rights, and entail encroachments on his or her freedom of conduct […]."[34]

Comparable endangerment situations can be identified in relation to biobanks. Donors who provide samples and data disclose extensive and sometimes sensitive information on their person and therefore deserve particular protection of their rights of personality. This is all the more the case in that they permit access not in their own interest, but for altruistic reasons, in a different way than in the usual contact with professional persons who generally have a duty of professional discretion and a right to refuse to give evidence and are subject to a prohibition of seizure. By reason of this altruism, they can all the more expect that the persons who have the de facto power of disposal of samples and data observe secrecy towards third parties with regard to this information and cannot be forced to disclose it against their will. Where this is not sufficiently guaranteed by statute, this undermines the confidence and thus also the willingness to donate of the persons whose samples and data are essential for science.

At the same time, the constitutionally guaranteed freedom of research under Article 5(3) of the Basic Law suggests that data traffic within the domain of research should be given particular privileges and should be separated from other (non-academic) domains. In this process, the relevant groups of persons who work within the domain of science cannot be defined by occupational characteristics, but follow from their functional relationship to the structure and operation of a biobank. From this point of view, all persons who have de facto access to data keys and identifying data should be included in the group of persons with a duty of biobank secrecy. In a sense, they manage access to the possibility of personalizing the stored samples and data. On account of the increasing

34 BVerfGE 120, 274 (312 ff.); for English translation, see the Court's website: http://www.bundesverfassungsgericht.de/entscheidungen/rs20080227_1bvr037007en.html [2010-09-27].

possibility of re-identifying anonymized samples and data, the group of persons with a duty of biobank secrecy must, finally, also include all persons who have access to anonymized and pseudonymized samples and data.

Right to refuse to give evidence and prohibition of seizure

As stated above, biobank secrecy should also include a right to refuse to give evidence and a prohibition of seizure based on this. It is true that in the year 1972 the Federal Constitutional Court stated that every extension to new groups of persons of the criminal procedure right to refuse to give evidence restricted the possibilities of the prosecution authorities and therefore possibly had an adverse affect on reaching a substantively correct decision. In this respect, the interest in an operational administration of criminal justice, which is contained in the principle of the rule of law, set limits to expanding at will the group of persons with a right to refuse to give evidence.[35]

However, the court certainly recognized the need for an expansion of the group of persons with a right to refuse to give evidence. Later amendments of section 53(1) sentence 1 of the Code of Criminal Procedure added further groups of persons whose occupation requires them to deal with sensitive information, for example drugs counsellors and psychotherapists. And if the legislature created a right to refuse to give evidence for persons who deal with biobank materials and data, it would also be complying with its particular mandate of protection of personal data. For biobank secrecy which includes a right to refuse to give evidence is justified for the protection of the general right of personality and the right to informational self-determination under Article 1 in conjunction with Article 2 of the Basic Law.

Health data are generally sensitive data. This applies to a greater extent to genetic data, for if these are combined with other data which are collected in epidemiological studies, persons

35 BVerfGE 33, 367 (383). The principles developed there became part of established case law, cf. BVerfGE 36, 193 (203, 211); BVerfGE 38, 312 (321); BVerfGE 44, 353 (378); BVerfG, decision of 18 January 1996, 2 BvR 2886/95, NJW 1996, 1587.

in a sense become "transparent". This touches on the core area of human life, privacy and the right to informational self-determination. The objection is made that the donors or patients voluntarily disclose their data, that is, without hindrance they effectively exercise their right to informational self-determination, but this is countered by the fact that the individual, despite being giving information and declaring his consent, cannot assess who uses his data for what purposes, and in particular whether, when and how the state or other organizations can have access.[36]

Under the Code of Criminal Procedure, the right to refuse to give evidence is accompanied by a prohibition of seizure. Section 97 of the Code of Criminal Procedure provides for a fundamental prohibition of seizure if the objects are in the custody of persons who may invoke a right to refuse to give evidence under section 53 of the Code of Criminal Procedure.

Admittedly, the provisions on averting danger make access possible under less restrictive conditions than is possible in criminal prosecution. For the provisions on averting danger do not aim at convicting an offender in formalized proceedings, but serve the preventive protection of public security and order and thus of the rights and legal interests of citizens. The powers of authorities to avert danger, for example in the case of imminent danger to life or limb, are correspondingly more broadly drafted and extend further.[37]

Even in the field of averting danger, however, it is constitutionally problematical to give the state by statute access to the particularly sensitive data which are stored in biobanks solely

36 Cf. BVerfGE 120, 274 (312) – online searches; 118, 168 (184) – electronic eavesdropping.

37 Cf. section 20c(3) of the *Bundeskriminalamtgesetz* (Federal Criminal Police Office Act). In order to combat dangers to the state, life, limb or freedom, even persons with a right to refuse to give evidence, with the exception of criminal defence attorneys, clergymen and members of the *Bundestag*, may be required to give information. An example of broader provision is section 9a(2) of the *Polizeigesetz Baden-Württemberg* (Baden-Württemberg Police Act): Where there is immediate danger to life or limb, particular persons with a duty of professional discretion (e.g. doctors) have a duty to give information and must tolerate the seizure of objects in their custody.

for purposes of scientific research and for altruistic reasons.[38] At all events it is necessary to avoid the comparatively strict provisions of criminal prosecution being undermined in an attempt to avert danger. Consequently, statutory provisions for biobanks should expressly provide for an exclusion of evidence for the case where information is obtained in order to avert danger but the narrower requirements to enable it for be used for criminal prosecution are not satisfied.[39]

For practical reasons, the suitability of a biobank as a source of information for the work of the criminal prosecution and regulatory authorities may be questionable. At present, there is little likelihood of the sample or record of a criminal offender being stored in a biobank. In addition, the DNA patterns stored in scientific databases are different in structure from the DNA profiles which are prepared in forensic investigations. It is therefore at present impossible to make a direct comparison between the trace left by an offender (or a DNA profile prepared from body cells left by an offender) and the DNA profiles prepared in a research context. However, the investigations in connection with the murder of the Swedish Foreign Minister Anna Lindh showed that even in the past biobanks were certainly suitable for criminal prosecution.[40] It is all the more conceivable that there will in future be conditions under which biobanks will be more suitable for averting danger or for criminal investigations. At present biobank research is considering providing a definitive description of each stored sample by extracting a specific DNA pattern, in a similar way as this is done with the use of

38 On this, see in particular the recent decision of the Federal Constitutional Court on data retention: BVerfG, 1 BvR 256/08 of 2 March 2010, paragraph nos. (1-345). Online: http://www.bundesverfassungsgericht.de/entscheidungen/rs20100302_1bvr025608.html [2010-05-03].

39 Cf. section 20c(3) sentence 5 of the Federal Criminal Police Office Act, which provides that the information obtained may be used only to avert specific dangers. A similar provision, for example, is section 12(2) sentence 3 of the *Hessisches Gesetz über Sicherheit und Ordnung* (Hesse Act on Security and Order); this contains an express restriction of use to the purposes of averting danger; use in criminal proceedings of the knowledge obtained is excluded.

40 See fn. 19.

forensic DNA examinations. The motive for this is to improve quality assurance; this would avoid samples being mixed up or becoming unusable if the label is damaged.[41] If this were put into practice without exceptions and if biobank samples were characterized by a universally used DNA pattern, this would make it substantially easier for the regulatory and criminal prosecution authorities to use biobanks; it would then be possible for the same pattern to be extracted from traces at the scene of the crime and to be compared the patterns of samples in a biobank with the help of an automatic search procedure.

If such a procedure were possible, this would be equivalent to random checks of a large number of persons. The principle of proportionality must be observed in the necessary weighing of the interest of the state in averting danger and criminal prosecution and the interest of the donors in the protection of their highly sensitive personal data: The use of such data is a substantial encroachment upon the particularly protected sphere of the private lives of thousands of persons who are not under suspicion. The state should therefore show restraint, particularly since it has enough other means at its disposal. Protection of the donors should have priority.

Conclusions

Collectively, biobank secrecy must satisfy the following requirements:

a) It must apply for the duration of existence of the samples and data from the time when the samples are acquired and the related data are collected.
b) It must restrict the processing and transfer of samples and related data for the duration of their existence to the purposes of scientific research.

41 Cf. Pakstis, A. J. et al.: SNPs for a universal individual identification panel. Human Genetics 127, 3 (2010), 315-324; Pakstis, A. J. et al.: Candidate SNPs for a universal individual identification panel. Human Genetics 121, 3-4 (2007), 305-317.

c) It must guarantee that they are inaccessible to all non-research third parties and ensure this by appropriate prohibitions on use.
d) It must enable and at the same time guarantee the use of anonymized and pseudonymized samples and data in accordance with their intended use and their further transfer for this use alone.
e) Personal samples and data may be transferred within the domain of science only to the extent that this is necessary for research purposes.

Biobank secrecy in the meaning set out above can be introduced only by statute.

EU law does not conflict with such a statute. In the EU, provisions to safeguard data protection, at all events outside the public area, have a common basis, the 1995 EC Data Protection Directive[42], which therefore also permits unhindered data exchange. This directive, however, does not provide for secrecy of research, any more than do the provisions applicable in the other Member States. It is also clear that the provisions of the directive are favourable to research but at the same time require particular guarantees for the protection of the persons affected. Biobank secrecy fits this requirement perfectly and is therefore in compliance with the directive.

4.2.2 Defining permissible use

Requirement of consent

In principle, legitimation for the use of human bodily substances and related data may be attained in two ways, either by

42 Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data. Online: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31995L0046:EN:HTML [2010-06-19].

legislation or by the consent of the individual donor. Legislation has the advantage that it lays down the powers to use the samples and data in abstract and general terms and thus gives research a high degree of legal certainty and uniformity. But this meets with the objection that the associated government encroachment upon rights of personality, in particular upon the donors' right to informational self-determination, can scarcely be justified. There may be good reasons why someone does not wish to make his samples and data available for research or at least not for particular research. Such a decision falls within the definition of "privacy and freedom of conduct", which according to the argumentation of the Federal Constitutional Court cited above (cf. 4.2.1) is protected in terms of fundamental rights. For this reason, it is recommended that the fundamental requirement of consent of the donor in question be adhered to.[43] This applies all the more to obtaining bodily samples from a person.

The requirement of consent should also apply in general to samples and data which are to be entered in a biobank only after a planned anonymization or pseudonymization. The donors' consent must also be obtained where a collection narrowly defined in topic and duration for which no transfer to third parties is planned is to be integrated or converted into a biobank without such restrictions.[44]

Limitation of use to a specific purpose

Not only the consent itself but also its scope is of central importance for the work of a biobank. On giving his consent, the donor not only gives authorization for use, but also binds

43 This Opinion does not further discuss the problem of the consent of persons who do not have capacity to consent. In this respect, reference is made to the Opinion "Biobanks for research" of the German National Ethics Council (72 ff.; cf. fn. 1) and the report of the Study Commission on Law and Ethics of Modern Medicine (329 ff.; cf. fn. 4).

44 For old samples which were obtained before statutory provisions on biobanks entered into force, the German Ethics Council refers to the general data protection law and to the Opinion of the German National Ethics Council (cf. fn. 1).

this authorization to specific purposes. On condition that the donor was sufficiently clearly informed on this and that he consented on this basis, it should be possible for his samples and the data related to them to be used without restriction to a specific research project or a specific field of research for an indefinite period of time for scientific research. At the same time the donor should have the possibility of excluding individually specified uses which he does not wish to consent to. Admittedly, the biobank operator may refuse the donation of samples which are limited to specific purposes in a way it regards as too narrow.

In order to safeguard the limitation of use to a specific purpose, the donor must also be permitted at any time to revoke his consent to the use of samples and data, and he must not be permitted to waive this right of revocation. Of course, the revocation can relate only to identifiable samples and data which have not yet been anonymized. In addition, there should be no obligation to destroy research results that have already been obtained, provided that the data are contained therein only in aggregate form and without any relation to a person. In addition, it should be possible to agree with the donors that in the case of a revocation of consent, samples and data must only be anonymized, not destroyed; however, it must be clearly explained to the donor in this circumstance that in many cases an absolutely watertight anonymization is not possible.

The limitation of use to a specific purpose must be structured by statute or contract in such a way that not only the biobank operators are bound by it, but also all persons who have access to the samples and data. On the technical level, such a "concurrent" authorization of use in the form of *tags*[45] directly linked to the data can ensure that every time the data are used the relevant information is directly available and that

45 In information technology, the term *tag* refers to marking a data record with additional information, which may serve very different purposes depending on the field of use. *Tags* are therefore meta-information, additional information on data, which give details of their origin and/or purpose of use.

when biobanks or individual samples or data are transferred, this information is also directly transferred with them.

Providing donors with information

Although, as set out above, the requirements of the donor's consent should be adhered to, the biobank secrecy that is called for permits the requirements as to *informing* the donor on possible future research projects to be restricted. For to the same degree to which he can justifiably rely on his samples and data not being misused, he can – provided he so wishes – waive the right to detailed information, as an indication of his trust. In other words, the degree of information may be decreased to the same extent to which the person affected is spared the need to monitor, because the duty of monitoring is transferred to other institutions and safeguarding mechanisms. This means:

Provided the (potential) donor makes his consent dependent on specific information, he must either be given this information or the biobank must do without the use of his samples or data.

Apart from this, it is enough if he is given sufficient information on the tasks of the biobank and possible transfers to third parties. This includes the following:

a) that sample donation is voluntary,
b) the organization responsible for the biobank,
c) that the samples will exclusively be used (and transferred) for the purposes of scientific research, which may include a later commercial use of the research results,
d) the occasions and procedures for the donor to be contacted again in the future
   - to collect further data,
   - to obtain extended consent,
   - to report on individual research results,
e) the anonymization and pseudonymization of samples and data,

f) reference to the possible transfer of samples and data, perhaps abroad, in Europe or outside Europe,
g) the right to restrict consent to the use of samples and personal data and to revoke it,
h) the whereabouts of samples and data on revocation of consent and if the biobank is terminated.

4.2.3 Involving ethics commissions

For research on human beings or with personal data, a large number of provisions[46] provide that an ethics commission should be involved; some merely provide a duty of consultation, and some additionally provide for the duty to obtain approval. The provisions often do not cover research with biobank materials.

Where biobank secrecy applies, it is not necessary to provide for the approval of an ethics commission for every individual research project which is to work with biobank samples or data. Biobank secrecy averts a large proportion of the endangerment of donors' personality rights that is entailed by biobank research. It protects the samples and data against external access and prevents them being used for purposes other than research.

In the case of collections that are not restricted in topic and duration, further safeguarding is necessary. Firstly, the biobank must be subjected to a system evaluation.[47] Secondly, there should be a periodic evaluation of the activities of the biobank by an ethics commission on the basis of a report which gives detailed information on the past biobank activities including

46 For certain cases (medicinal products research, medical devices research, research using radioactive materials or ionizing radiation), it is laid down by statute for particular occupations (e.g. doctors) by professional ethics regulations, or for members of particular organizations (e.g. members of universities) by the charter and institutional law of the relevant institution or by guidelines of research funding institutions, that there shall be ethics commissions with interdisciplinary members, where research on human beings and/or research using personal data is involved.

47 Cf. schedule to section 9 of the Federal Data Protection Act.

the projects carried out. The evaluation of the biobank activities, in combination with measures to safeguard transparency (see 4.2.5) will induce the biobank operators to prohibit ethically problematic research using the samples and data available in the biobank.

The approval of an ethics commission *before* a research project is carried out is in all cases necessary if the researchers wish to work with personal samples and data which are not pseudonymized, or if it is intended to contact the donor again. In both cases there is a particularly intense encroachment upon the donor's rights of personality, which necessitates a preceding ethical and legal assessment.

However, this requires the instruction of the ethics commission to include the appropriate competence, which at present is not always the case. In this respect, those institutions that lay down the competence of the ethics commission in question must ensure that the competence is correspondingly extended. In addition to the ethics commissions which have local competence for a biobank, however, the ethics commissions which are competent for the researchers involved should also become involved in consulting on biobank projects.

4.2.4 Quality assurance

In processing personal data, biobanks assume responsibility for data security. The measures to be taken must safeguard the donors' personality rights for the complete existence of samples and data, that is, from the date when they are collected until the date when they are destroyed. For this purpose, the following conditions must be fulfilled:

a) Samples and data must be effectively protected against abuse by appropriate technical and organizational measures.
b) As early as possible, but at the latest when they are entered in the biobank, there must be a separation of the data which

identify the persons affected on the one hand and the samples and other data on the other hand.

c) The operators of the biobank must lay down clear regulations for access to and use of samples and data.

For biobanks which are not restricted in topic and duration, further quality assurance measures must be established in connection with data protection. Quality assurance aims at determining and reviewing the suitability of data protection measures for the intended goal and ensuring their quality in the long term. One possibility of quality assurance, for example, is having the biobank's data protection concept examined and evaluated to establish whether it is compatible with data protection provisions (data protection audit). Another possibility is conducting regular random reviews of the biobank.

d) For this purpose it is necessary to create rules for the structure of and procedures in the biobank.

e) The data processing must be made transparent. The foundation for this is complete documentation
   - of the origin of the samples and data stored, their purpose of use, the groups of persons entitled to access and the conditions for access,
   - of accesses to samples and data,
   - of transfer of samples and data; the transfer of samples and data and the terms of their use by third parties (the recipients of the samples) must be fully documented and laid down in a transfer contract (Material Transfer Agreement).

f) In addition, the responsibilities in the domain of data protection must be clearly defined; here, conflicts of roles must be avoided.

g) A condition to enable transparency is the introduction of standard operating procedures, SOPs, in order to guarantee that activities relevant to data protection are carried out uniformly.

4.2.5 Transparency

Transparency requires that all biobanks have a complete documentation of the way the relevant samples and data are processed, as is today already good scientific practice.

However, biobanks which are not restricted in topic and duration have further requirements, for transparency is an important supporting instrument here to protect donors' interests. It is the foundation of potential supervision, since it makes processes of collection, storage and transfer of samples and data clearly visible. Apart from this, transparency also indirectly serves the interests of the researchers, since it is likely to increase the willingness of donors to cooperate.

The requirement of transparency defined in this way refers to the procedural and institutional structure of biobanks which are not restricted in topic and duration. In view of the purpose of use of biobank samples and data, which cannot be specified in detail in advance, the donors must have the possibility for the complete duration of use of the samples and data to understand the procedures of collection, storage and transfer, and also the research purposes for which individual samples and data are used, in order, for example, to exercise their right of revocation. Guaranteeing transparency in the long term can largely compensate for the restricted information given to the donors at the date when they give their consent.

Transparency should in concrete terms be guaranteed by the following precautions:

a) the establishment of a public biobank register with information on the contents and organizational structure of the biobank,
b) public access (e.g. through an internet portal) to
   - details of on the legal form, agencies responsible for data protection law, data protection officer, competent supervisory authorities,
   - details of competencies in the biobank's organization,

- details of contact persons and possibilities of obtaining fuller information,
- a clear and generally intelligible account of the regulations on the collection, use and transfer of samples and data,
- a clear, generally intelligible and up-to-date account of the purposes for which samples and data have been used or transferred,
- regular publication of generally intelligible reports on the activities of the biobank,[48]
- regular publication of reports on quality assurance measures.

4.3 Ensuring donor protection internationally

International cooperation also requires the possibility of transferring the samples and data contained in domestic biobanks outside Germany. This is normally done in pseudonymized or anonymized form.

However, the transfer of pseudonymized samples and data may entail substantial complications if the foreign legal system does not offer a level of protection equivalent to that in Germany. Provisions established in Germany for biobanks may therefore possibly lose their effect. With regard to biobank secrecy, the danger might then exist that a foreign authority which had accessed biobank materials and data under its own law transferred the information thus obtained to German criminal investigation authorities and these used the data for criminal prosecution.

There are several measures to safeguard against this: Firstly and primarily, there should be a strict separation of biobank

48 This does not mean that all donors – possibly without making a request – are to be informed on the individual data obtained with the use of their samples. On the communication of research results to the donor, see German National Ethics Council 2004, 15, 59 f. (cf. fn. 1).

materials and data on the one hand and reference lists which can be used to allocate the pseudonymized samples and data to the relevant donors on the other hand. The reference lists, or the connections to personal data contained in them, should not be permitted to be transferred abroad.

Secondly, it should be specified that the persons who deal with samples and data should before receiving them at all events agree to observe biobank secrecy, provided this is permitted by their respective legal systems. If it is not possible for them to enter into this agreement, the biobank must examine whether in the individual case transfer should be refused on account of danger to donor protection.

Thirdly, where a state has access, biobank secrecy should be protected against differences in legal systems in such a way that information obtained by foreign access to samples and data is at all events inadmissible as evidence in criminal proceedings in Germany where there would have been no lawful right of access to the samples and data in Germany.

Germany should take the initiative in creating internationally uniform protection standards for biobank materials and data. Where the transfer is to take place within the European Union, there is every reason to involve the bodies within the EU which are responsible for research and data protection at the earliest possible date, in order to achieve an explicit and Europe-wide recognition of biobank secrecy.

Beyond the borders of the EU, an international convention on the requirements for the use of personal samples and data for research purposes should be proposed; this convention should also concern itself with biobank secrecy. There are first signs of this in the recommendation of the Council Europe on research with human biological material[49] of 2006 and in the current consultations of the OECD, although these are to

49 Council of Europe Committee of Ministers (ed.): Recommendation Rec (2006)4 of the Committee of Ministers to member states on research on biological materials of human origin. Online: https://wcd.coe.int/ViewDoc.jsp?id=977859 [2010-05-27].

date only the preliminary stage of a planned recommendation (Recommendation on Human Biobanks and Genetic Research Databases, July 2009).

5 SUMMARY AND RECOMMENDATIONS

Summary

Human biobanks usually refers to collections of samples of human body substances (e.g. tissue, blood, DNA) which are linked to personal data and socio-demographic information about the donors of the material. They have a dual nature as collections of samples and data. Most currently existing biobanks are research biobanks, that is, systems which collect samples and data of human origin and either use these for their own research or make them available to third parties for research purposes. They play a central role in research on the causes and mechanisms of a large number of illnesses and their treatment and are a vital resource for biomedical research and are frequently designed to be used for various research purposes, some of which only arise at a later date.

Biobanks raise ethical and legal questions which extend from the protection of individual rights to the global control of research infrastructures. The *Gesetz über genetische Untersuchungen bei Menschen* (Human Genetic Examination Act, also known as Genetic Diagnosis Act), which entered into force in February 2010, contains no provisions on these questions. Section 2(2) provides that the Act does not apply, amongst other things, to genetic examinations and analyses that are undertaken for research purposes. As a result, there are at present no specific statutory provisions for biobanks in Germany.

Both the former German National Ethics Council[50] and the Study Commission[51] of the *Bundestag* have considered biobanks in earlier opinions. Since that time, however, there has been more dynamic development in this area. Not only

50 German National Ethics Council 2004 (cf. fn. 1).
51 Study Commission on Law and Ethics of Modern Medicine 2002 (cf. fn. 4).

are new biobanks constantly being established, but they are used in new forms and dimensions, which makes it necessary to consider the subject again. The new developments include quantitative expansion, a greater degree of information contained, the increasing possibility of re-identification of donors, an increasing tendency towards networking, internationalization, privatization and commercialization, and the expansion of the purposes of use and third-party access.

These developments make it necessary for current legislation to be adapted to the new circumstances.

Against the background of the deliberations made and criteria developed in this Opinion, the German Ethics Council sets out below a number of recommendations for implementing the five-pillar concept described above. These recommendations do not cover all the aspects to be taken into account in connection with the establishment, operation and organization of biobanks. With regard to the questions not dealt with in this Opinion, reference is made to the earlier Opinion of the German National Ethics Council mentioned at the beginning.

I. General recommendations

I.1 The German Ethics Council recommends that statutory provisions on human biobanks for research (hereinafter referred to as biobanks) should be passed; these should take account of the specific requirements of the legal protection of the samples and data contained in biobanks.

I.2 These recommendations should cover every collection which satisfies the following three criteria:

a) It is a collection of human material containing genetic material with associated data.
b) Its samples are electronically linked to personal information (sometimes pseudonymized) and further information, in particular relating to health.

c) Its samples and data are collected, preserved or used for purposes of scientific research.

I.3 The German Ethics Council recommends that collections that are narrowly defined in topic and duration and for which there are no plans for transfer to other agencies within the meaning of data protection law should be released from the following recommendations II.3 c), II.4 b), II.5 b) and II.5 c). Should such a collection be transferred to or converted into a biobank without such restrictions, there must be consent to this from the donors, and the donors must be informed of the whereabouts of their samples and data.

II. Recommendations for a five-pillar concept

II.1 Biobank secrecy

Biobanks, as a resource for scientific research, cannot be narrowly limited to specific purposes in the use of samples and data. Nor is it usually possible to inform the donors in advance of the precise purposes of use and of the duration of storage and use. Both these deficiencies should be compensated for by legislation that use should be exclusively for scientific research, together with biobank secrecy.

The provision for biobank secrecy must satisfy the following conditions:

a) It must apply for the complete duration of existence of the samples and data from the time when the samples are acquired and the related data are collected.
b) It must restrict the processing and transfer of samples and related data for the duration of their existence to the purposes of scientific research.
c) It must guarantee that they are inaccessible to all non-research third parties and ensure this by appropriate prohibitions on use.

d) It must enable and at the same time guarantee the use of anonymized and pseudonymized samples and data in accordance with their intended use and their further transfer for this use alone.
e) Identifiable samples and data may be transferred within the domain of science only to the extent that this is necessary for research purposes.

The wording of biobank secrecy must protect in more than one direction; there are models for this in current law, but as yet no specific provisions for biobanks:
f) Biobank secrecy must include a duty of professional discretion: It must be prohibited to transfer personal samples or data to persons and agencies outside the domain of science. The target group of this duty of confidentiality includes not only the operators and employees of the biobank, but also the researchers and their assistants who use the information.
g) All persons who work with anonymized or pseudonymized biobank materials must be prohibited from taking measures to identify the donor.
h) External private agencies (e.g. insurance companies, employers) must be subjected to a prohibition of the use of personal information which is obtained with the use of biobank materials.
i) Persons who have a duty of professional discretion must be granted a right to refuse to give evidence in court and at other state agencies; supporting this, there must be provision for a prohibition of seizure of the samples and data subject to biobank secrecy. Any knowledge that is acquired in the course of warding off danger must be subject to a prohibition on use in criminal proceedings.

II.2 Defining permissible use

a) The essential requirement for the use of the samples and data in biobanks should be the donors' consent.

b) Donors must be given sufficiently clear information as to whether their samples and data are to be used without restriction to a specific research project or a specific research field for an indefinite period of time for scientific research.
c) The donors should have the possibility of excluding specific fields of research or measures from their consent.
d) The limitation of use to a specific purpose must be structured by statute or contract in such a way that not only the biobank operators are bound by it, but also all persons who have access to the samples and data. The terms of use, together with the consent, should be connected directly to the data, so that the relevant information is available every time the biobank is used, and they should automatically be transferred together with biobanks or individual records or samples which are transferred to other institutions.
e) In order to safeguard the limitation of use to a specific purpose, the donor must also be permitted at any time to revoke his consent to the use of samples and data which have not yet been anonymized, and he must not be permitted to waive this right of revocation. However, there should be no obligation to destroy research results that have already been attained, provided that the data are contained therein only in aggregate form and without any relation to a person. In addition, it should be possible to agree with the donors that in the case of a revocation of consent, samples and data must only be anonymized, not destroyed; however, it must be clearly explained to the donor in this circumstance that in many cases an absolutely secure anonymization is not possible.
f) The requirement of consent should also apply in general to samples and data which are to be entered in a biobank only after a planned anonymization or pseudonymization.

II.3 Involving ethics commissions

a) Where biobank secrecy applies, it is not necessary to provide for the opinion of an ethics commission for every

individual research project which is to work with biobank samples or data.

b) However, the approval of an ethics commission should be necessary if work is to be done using personal samples and data from a biobank or it is intended to contact donors again.

c) The activities of biobanks which are not restricted in topic and duration, including the projects carried out with their samples and data, should be periodically evaluated by an ethics commission with regard to their ethical defensibility on the basis of reports on the biobank.

II.4 Quality assurance

a) The technical and organizational measures provided for biobanks must be suitable to guarantee the rights of the donors for the complete duration of the existence of the samples and data. Appropriate organizational structures and procedures including clear allocation of responsibility, also taking account of compliance with data protection law, must be provided for.

b) In order to ensure that these precautions are taken, biobanks which are not restricted in topic and duration must be subjected to a system evaluation. The procedure and time limits for this must be specified by statute.

II.5 Transparency of aims and procedures of a biobank

a) The use of samples and data should be documented in full.

b) A public biobank register should be established, containing information on the contents and organizational structure of biobanks which are not restricted in topic and duration.

c) Every biobank which is not restricted in topic and duration must provide the following information in a publicly accessible form (e.g. on an internet portal):

- details of the legal form, agencies responsible for data protection law, data protection officers, competent supervisory authorities,

- details of competencies in the biobank's organization,
- details of contact persons and possibilities of obtaining fuller information,
- a clear and generally intelligible account of the regulations on the collection, use and transfer of samples and data,
- a clear, generally intelligible and up-to-date account of the purposes for which samples and data have been used or transferred,
- regular publication of generally intelligible reports on the activities of the biobank,[52]
- regular publication of reports on quality assurance measures.

III. Ensuring donor protection internationally

III.1 Both on the EU level and internationally, there should be an attempt to achieve binding standards of protection.

III.2 Where the level of protection abroad is not comparable to that in Germany, cooperation with researchers or with research institutions abroad should be carried out only subject to the following conditions:

a) There should be a strict separation of biobank materials and data on the one hand and reference lists which can be used to allocate the pseudonymized samples and data to the relevant donors on the other hand. The reference lists, or the connections to personal data contained in them, should not be permitted to be transferred abroad.
b) It should be specified that the persons who deal with samples and data should before receiving them at all events

52 This does not mean that all donors – possibly without making a request – are to be informed on the individual data obtained with the use of their samples. On the communication of research results to the donor, see German National Ethics Council 2004, 15, 59 f. (cf. fn. 1).

agree to observe biobank secrecy, provided this is permitted by their respective legal systems. If it is not possible for them to enter into this agreement, the biobank must examine whether in the individual case transfer should be refused on account of danger to donor protection.

c) Where a state has access, biobank secrecy should be protected against differences in legal systems in such a way that information obtained by foreign access to samples and data is at all events inadmissible as evidence in criminal proceedings in Germany where there would have been no lawful right of access to the samples and data in Germany.

SUPPLEMENTARY POSITION STATEMENT

We unconditionally support the aim of the German Ethics Council to find new forms of legislation for biobanks which are designed to use the scientific potential of cell and tissue samples containing genetic material in the long term and beyond their primary intended purpose and to link them to personal records.

However, we recommend that classical projects with a specific purpose and duration for which there are no plans to transfer samples and data for different uses should not be covered by the proposed regulations and should be clearly distinguished. The present provisions for these biobanks on the protection of data and donors when samples are taken are sufficient. In addition, there is the duty of professional discretion as part of doctor/patient confidentiality, and in the case of scientists who are not doctors there is the possibility of binding them by way of declarations of undertaking.

The German Ethics Council recommends provisions varying in detail, but we fear that if this is implemented, it will entail substantial regulatory and administrative expense. The many thousand small and restricted collections of samples for academic projects in connection with university dissertations and theses should be spared this expense. They should not be included as biobanks within the meaning of the Opinion, but should be distinguished from them.

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