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Biobanks for research

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Preface

The topic of this Opinion might initially appear somewhat arcane, of relevance only to certain experts. So why, it may be asked, has the Swiss National Advisory Commission on Biomedical Ethics taken up this issue, rather than leaving it to be discussed by the professionals concerned? The answer lies in the significance of the topic – which has yet to be appreciated by the public.

Biobanks for research are a new, but increasingly important institution within the healthcare system. Over the past few years, biobanks (some public, some private) have been established around the world and notably also in Switzerland. These collections of biological materials linked to donors' personal data make it possible for medical, pharmacological and biological research – known to be particularly advanced in Switzerland – to identify associations between the genome and serious conditions such as cancer, Alzheimer's or diabetes. However, the obvious opportunities are accompanied by considerable risks – in particular, risks to privacy and risks of discrimination.

In defining the opportunities and risks involved, there is a need for a broad public debate and, where appropriate, new legal regulations. With this Opinion, the Commission aims to raise awareness of the issue of biobanks for research in the Federal Council and Parliament, and especially among the public, and to stimulate debate and offer guidance.

As the topic of biobanks is still unfamiliar to many people, the Opinion begins by introducing and clarifying the concept, before discussing in detail the medical, social and (numerous) ethical aspects. The relationships between donors and biobanks and between biobanks and researchers are then explored and, on this basis, following the conclusions, five recommendations are made:

(1) donors' autonomy should be strengthened, (2) the data collected should be more effectively protected, (3) the legal framework should be improved and (4) biobanks should increasingly be obliged to serve the common good. Finally, (5) the recommendations should be implemented in the form of amendments to legislation and ethical guidelines, and public debate on biobanks should be promoted.

This Opinion is the eighth to be issued during my tenure as Chair of the Commission. Earlier Opinions addressed topics such as advance directives, presumed consent, "intersexuality" and medically assisted reproduction. In addition, Opinions on the culture of death and dying and on non-invasive prenatal testing (NIPT) are currently being prepared.

The preparation of the present Opinion involved initial plenary discussions, expert hearings, the production of drafts by a working group, further plenary discussions and the joint elaboration of a final – unanimously adopted – version.

For their dedication – as ever – and broad expertise, I would like to express my gratitude to all the members of the Commission and to the NEK-CNE Office; particular thanks go to the members of the working group and its indefatigable Chair, Bernhard Rütsche.

Bern, December 2015 Otfried Höffe, Chair

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1. Introduction

1.1 Significance of biobanks

1 Biobanks are an important new institution within the healthcare system. In recent years, largely unnoticed by the wider public, numerous biobanks have been established both in Switzerland and around the world. For **biomedical research**, and for genome research in particular, biobanks have become indispensable. While attention is focused on the links between the genome and diseases such as cancer, Alzheimer's or diabetes, biobanks are also a significant element of research infrastructure for applied studies on the relationship between genetic information and the effects of medicines or environmental influences.

2 Biobanks for research are collections of **biomaterials**, such as tissue, blood, DNA or proteins, which are linked to the donors' data – especially clinical and epidemiological data – and are typically used for a large number of research projects. Biomaterials are of interest for research primarily as carriers of **biological information**. Information of this kind can be collected as such, e.g. in the form of genetic data sets or as protein and blood measurements. Whether a collection is to be classified as a biobank cannot depend on whether the biomaterials are stored as physical substances or transcribed into data sets. In either case, however, one can only speak of a biobank if the biological data is linked to other donor data, particularly medical records.

3 In Switzerland and in other countries, a **wide variety** of biobanks now exist – public and private, non-profit and commercial. Among the largest are population-based collections of samples from hundreds of thousands of people – for example, the UK Biobank (cf. Box 4) or, in this country, the recently established Lausanne Institutional Biobank (BIL, cf. Box 1). There are also disease-specific biobanks, such as the International Cancer Genome Consortium (cf. Box 5), or biobanks for research on rare diseases. In addition, pharmaceutical companies hold extensive collections of biological materials and data deriving from clinical trials. Biobanks may be established for diagnostic or therapeutic purposes and additionally used for research; this is true, for example, of Pathology Institute tissue banks at University and central hospitals (cf. Box 2), cord blood banks, or the samples and data stored by medical laboratories. Biobanks are also maintained by private suppliers of genetic tests – e.g. 23andMe (cf. Box 11), Geni Family Tree or MyHeritage – if the test materials are stored and made available for research.

4 Biobanking involves **tensions between a variety of individual and public interests**:

– On the one hand, there are the interests of biomedical research in generating fundamental scientific knowledge and, over the longer term, the needs of current and especially future patients and healthcare professionals who hope to see new and more effective treatments developed. Accordingly, many donors wish to make a contribu-

tion to research either for altruistic reasons or out of solidarity with their own group of patients. Also at stake are the economic interests of companies within the biotech, medtech and pharma sector, as well as more general interests in strengthening the research location and improving the healthcare system.

– On the other hand, biobanks affect the rights and interests of the individuals whose samples and data are held, as well as the interests of their relatives. Of particular relevance are the donors' right to self-determination and the right to know or not to know in relation to genetic predispositions to disease and other health-related findings, as well as issues of data protection and data security. From the donors' perspective, data protection in particular is of crucial importance, as the misuse – e.g. by health insurers or employers – of highly sensitive personal data stored in biobanks could cause considerable harm to the donors concerned.

1.2 Science and society

5 The creation of biobanks is closely connected to the development of **personalised medicine**. The main goal of personalised medicine is to produce more effective treatments, more precisely tailored to individual patients; this is to be achieved – thanks to advances in genetic analysis and bioinformatics – by linking vast amounts of genomic data to individual data on health (diseases, therapies, etc.) and other personal data (lifestyle, diet, physical activity, income, etc.). This development has been described as a paradigm shift (German National Academy of Sciences Leopoldina et al. 2014) or even a revolution in medicine (D'Abramo 2015; Shaw 2015).

6 However, personalised medicine is still in its infancy (Emmert-Streib 2012). Indeed, some authors have called into question the **epistemological foundations** of this new field of scientific research – in particular, the relevance of genome sequencing for clinical practice and public health – asking whether genome screening of asymptomatic individuals for common conditions is actually beneficial (Cho 2015; Joyner & Paneth 2015).

7 Regardless of this scepticism, biobanks today already pose challenges for society, including **risks of social discrimination**. Together with other types of data collection, biobanks provide a basis for large-scale programmes of predictive health analysis. With such analyses, it may be possible to identify patients who are at high risk for complications following certain surgical interventions (Prainsack 2015), or when certain drugs are used, and who could therefore give rise to additional costs. Particular groups of patients could be favoured by researchers because they are better represented in hospital biobanks – in the US, for example, 92% of participants in genome-wide association studies (GWAS) are white, while only 8% belong to a minority ethnic or racial group (Ngui, Warner & Weiss Roberts 2015). At the same time, other groups could face stigmatisation because of the results of genetic research – and researchers and journal edi-

tors would therefore have to consider the acceptability of publishing information that could be harmful for the participants or their communities (Ngui, Warner & Weiss Roberts 2015). Other patients, again, could be advantaged because they are better organised or simply as a result of their genetic characteristics, their disease, or sectoral trends in scientific research. In other words, certain social groups might not enjoy the benefits of genetic research, and inequalities in health would be increased as a result.

8 Other challenges concern the **economic costs**. While, in the long term, personalised medicine could lead to a reduction in healthcare costs (through the development of more effective, targeted treatments), the infrastructure required for this purpose is already causing considerable costs. In most cases, biobanks are subsidised by public funds. In 2013, the Swiss National Science Foundation issued a call for concepts for the development of a new Swiss Biobanking Platform (cf. Box 3), offering CHF 3.2 million in funding. With a budget of EUR 140 million, the European authorities financed the Biobanking and BioMolecular resources Research Infrastructure (BBMRI), which was launched in January 2014 and comprises around 20 million samples (Stolz 2014). However, the investments required for the establishment of biobanking infrastructure are only the first step; this is followed by sequencing, analysis and exploitation of the results obtained. By way of example, the BIL has recruited 17,500 patients to date, and the costs of whole-genome sequencing for 20,000 samples are estimated at CHF 20 million (Nicollier 2014).

9 The **commercial use** of biobank data represents another major challenge for society. Relationships between industry and biobanks are inevitable and indeed – for the development of pharmacogenomics, which requires substantial investments – indispensable. However, such ties may give rise to mistrust among parts of the population. It is therefore important that the consequences of commercial involvement in biobanks – with regard to the sharing of risks, but also the individual and collective benefits – should be openly discussed (Hirschberg, Kahrass & Strech 2014).

10 The societal challenges associated with biobanks raise the question of democratic legitimacy and the engagement of citizens in their governance. Given that the decisions of the parties directly involved (donors, researchers, scientific bodies, executives, industry, etc.) affect broader groups or even the population as a whole, biobanks assume a **political dimension**. Accordingly, citizens should be informed about the key elements and implications of biobanks, so that these can become a matter of public debate and hence a project of society – not just of individual experts from research and industry.

1.3 Current state of debate and regulation

11 At the **international level**, the questions and challenges associated with the establishment and operation of biobanks have been discussed by experts for some years. In particular, the international debate has focused on the following ethical issues: donors'

informed consent to further use of their samples and data for research (acceptability of general consent), researchers' access to stored samples and data (data sharing), the security and confidentiality of samples and data, communication of the results of analyses to donors, publication of research findings, governance and transparency of biobanks, the sharing of benefits from commercialisable research results with donors and biobanks, and international cooperation of biobanks.

12 **Ethics commissions** in other countries (e.g. Germany, the UK, France, Austria) have considered the question of biobanks and published one or more opinions on this topic (German Ethics Council 2004, 2010; Austrian Bioethics Commission 2007, 2011; Comité Consultatif National d'Éthique 2003; Comitato Nazionale per la Bioetica 2006, 2014; Comité Consultatif de Bioéthique de Belgique 2009; European Commission 1998, 2012; Nuffield Council on Bioethics 2011, 2015; Danish Council of Ethics 2015). In addition, **international organisations** such as the Council of Europe, OECD, WHO and UNESCO have issued guidelines and recommendations, establishing standards for the collection, storage and use of biological materials and data for research (Council of Europe 2006; UNESCO 2003; WMA 2002, 2015). Certain **countries** (e.g. Iceland, Estonia, Sweden, Spain and Belgium) have introduced legislation on biobanks.

13 At the **national level**, guidelines and recommendations on the acquisition, storage and use of human biological materials in biobanks were published by the Swiss Academy of Medical Sciences (SAMS) in 2006. In view of the entry into force of the Human Research Act (HRA) at the beginning of 2014, the SAMS "Biobanks" guidelines were withdrawn. The draft version of the HRA included provisions on the operation of biobanks: large-scale biobanks were to be subject to mandatory authorisation, and others to mandatory notification. After the consultation procedure, these provisions were dropped; given the pace of developments in this area, legislators were concerned that regulations were likely to become outdated or unworkable within a short time (cf. Dispatch HRA, pp. 8083 f.; Gruberski 2013, p. 102). Accordingly, the Act and the associated Ordinances only regulate certain aspects of biobanking (in particular, questions of consent, duties of care with regard to the anonymisation and storage of biological materials and data, the prohibition of commercialisation, and authorisation requirements for research projects and, in some cases, for further use of materials and data for research purposes).

1.4 Aims and scope of the Opinion

14 In Switzerland, biobanks have not yet been the subject of a broad public debate. To date, the Commission has not expressed its views on this issue. The public's **trust** is a key "resource" for biobanks. Readiness to donate biological materials and to make personal data available for research may be drastically reduced if – even in only a small number of cases – materials and data are used for unauthorised purposes and such abuses come to light. To prevent misuse, effective safeguards are essential. At the same time, trust can be promoted by increasing public awareness of the nature and activities

of biobanks. Trust in an activity requires the greatest possible **transparency** with regard to the motives of the persons or organisations concerned, and the framework within which they operate. Transparency is also a fundamental requirement for public debate and for the democratic legitimacy which is indispensable given the significance of biobanks for society as a whole (marg. no. 10). Accordingly, the present Opinion aims to summarise the key facts for interested members of the public, and to discuss the central ethical and legal issues associated with biobanks.

15 At the same time, for policymakers and the administration, this Opinion seeks to identify the **need for action and regulation** with regard to the activities of biobanks in Switzerland – particularly given the fact that the SAMS "Biobanks" guidelines have been withdrawn and institutional regulations for biobanks were not included in the HRA. It needs to be determined whether a regulatory vacuum exists or, conversely, whether existing law impedes the development of biobanks through excessive regulation.

16 The Opinion only deals with biobanks which are (also) designed **for research**. It does not cover biobanks operating exclusively for diagnostic or therapeutic purposes – in such cases, the samples and data are used on behalf of, and for the benefit of, the patients concerned and are not intended to be transferred to third parties. In contrast, from the donors' perspective, biobanks for research (primarily) serve non-therapeutic purposes. In addition, the persons processing the samples and data (i.e. researchers) are not acting on the donors' behalf; for this reason, the latter cannot control how the samples and data are handled. However, biobanks operating in a diagnostic or therapeutic context are frequently also employed for research purposes; here, the term "biobank for research" is also applicable. Collections of biological materials maintained in departments of anatomy and medical history or in museums/exhibitions do not fall within the scope of this Opinion – unless such collections are also made available for research.

17 Discussion of the management of big data and databases in general would go beyond the scope of this Opinion. Of particular importance here are **health databases**, i.e. the ever-growing hoards of health-related data held by companies which specifically collect such data (e.g. raw data from pharmaceutical companies' clinical trials) or which acquire it in connection with the services they provide (e.g. Apple, Google, PatientsLikeMe; cf. Box 8). Health databases may also be utilised for biomedical research, either when data is made available for research projects, or when they are converted into biobanks for research. Health databases are thus confronted with ethical challenges similar to those faced by biobanks – particularly with regard to self-determination concerning data, data protection, data access for researchers and commercial use of data. Accordingly, the considerations relating to biobanks are also at least partly applicable to health databases.

2. What are biobanks?

2.1 Types of biobanks

18 As mentioned above (marg. no. 2), biobanks for research are collections of biological materials (samples), or data deriving from such materials, which are or can be linked to the donors' personal data, and which are made available, together with this data, for the conduct of research projects. In practice, numerous different types of biobanks for research exist.

Public and private biobanks

19 Firstly, public and private biobanks are to be distinguished. **Public biobanks** are sponsored by public institutions, specifically university hospitals, or operate with a public mandate and public funding. Examples include the Lausanne Institutional Biobank (BIL, cf. Box 1), the pathology institute tissue banks of university and central hospitals (cf. Box 2), and national biobanks such as those in the UK (UK Biobank, cf. Box 4), Denmark (Danish National Biobank[1]) or Estonia (Estonian Genome Center, EGC[2]). Public biobanks are typically non-profit organisations, offering a public service for the research sector. Therefore – unless they can pass on their costs to researchers – they have to be publicly funded.

20 As regards **private biobanks**, mention should be made, first and foremost, of the collections of samples and data maintained by pharmaceutical companies and clinical research organisations, mainly deriving from clinical trials. Collections of samples are also established by smaller biotech and life sciences companies to enable research on active substances. Biobanks may also be sponsored by private foundations such as the SCQM Foundation (Swiss Clinical Quality Management in Rheumatic Diseases) of the Swiss Society for Rheumatology, which operates a biobank containing serum and DNA samples from patients with rheumatic diseases (SCQM Biobank[3]). Some private biobanks operate on a commercial basis, charging researchers for access to their samples and data, or selling such material to other companies; this is true of 23andMe, a company supplying direct-to-consumer genetic tests (cf. Box 11). Usually, however, private biobanks (e.g. the SCQM Biobank) are also run on a non-profit basis. Overall, it can be assumed that most biobanks are not commercial enterprises, even though many such collections have arisen from private-sector initiatives.

21 In practice, **private-public partnerships** also exist, where private investors become involved in public biobanks or develop and operate biobanks in collaboration with pub-

1 http://www.biobankdenmark.dk/

2 http://www.geenivaramu.ee/en

3 http://www.scqm.ch/biobank

lic actors (Cambon-Thomsen, Rial-Sebbag & Knoppers 2007). Sometimes, biobanks are also set up on the initiative of **groups of patients**, who wish to facilitate research on their – often rare – disease by donating biomaterials. An early example of a patient-initiated collection is the Canavan Registry, which was established in the US in the 1990s by Ashkenazi Jews to facilitate isolation of the Canavan gene and the development of a genetic screening test. Canavan disease is a serious neurological condition, inherited as an autosomal-recessive trait and particularly prevalent among the Ashkenazi Jewish population. By providing samples and data, patient groups are now playing an increasingly active role in biomedical research.

Population-based and disease-specific biobanks

22 A further distinction relates to the donor population and the purpose of biobanks. **Population-based biobanks**, such as the major national institutions, collect samples from broad sections of the population, including healthy subjects as well as patients. The purpose of these large-scale projects is usually broadly defined (use of samples and data for biomedical or epidemiological research in general). In practice, however, there are also population-based biobanks established for more narrowly defined research purposes or for specific research programmes, where the donor population (cohort) is thus selected according to particular criteria. For example, in the cohort study known as SAPALDIA (Swiss study on Air Pollution and Lung Disease in Adults[4]), which was launched in 1991, blood and DNA samples were collected from several thousand subjects in eight regions representative of Switzerland's geographical diversity and varying environmental conditions, in order to investigate possible effects of air pollution on health.

23 In contrast, the samples held in **disease-specific biobanks** come from patients. Biobanks may be dedicated to a particular type of disease, such as cancer (e.g. the International Cancer Genome Consortium, cf. Box 5, or the Genotype-Tissue Expression project, GTEx[5]), mental disorders (e.g. the Psychiatric Genomics Consortium, cf. Box 6), or rheumatic disorders (e.g. the SCQM Biobank mentioned above). More generally disease-related are hospital biobanks, which store samples from patients along with their medical records for research purposes (e.g. the BIL, or pathology institute tissue banks). Such collections are more similar to population-based biobanks but generally do not contain samples collected from healthy subjects.

Acquisition of samples and data

24 In line with the distinction between population-based and disease-specific biobanks, there are differences in how samples and data are obtained. While population-based biobanks collect samples and data from healthy subjects **specifically for storage for**

4 www.sapaldia.ch/en/

5 http://www.gtexportal.org/home/

research purposes, disease-specific biobanks typically obtain samples and data in a **diagnostic or therapeutic context**. At the same time, it may be that biomaterials collected for analysis or treatment are (also) intended from the outset to be used for research. For example, on admission to Lausanne University Hospital (CHUV), patients are asked whether they consent to certain samples and data being transferred to the BIL.

25 But it is also possible that a collection originally established for **diagnostic or therapeutic purposes** may subsequently be made accessible for research or converted into a research biobank. This applies, in particular, to the tissue collections of pathology institutes. However, hospital repositories of blood samples from newborn screening programmes, cord blood or blood stem cell banks, and samples and data from laboratories conducting genetic and other medical analyses also have great potential for biomedical research.

26 A different situation arises in cases where samples collected **for a specific research project** are subsequently used for further research projects; here, probably the most important example would be collections of materials from clinical trials.

Linkage to personal data

27 Biobanks supply biological materials and data which are required for genome-wide association studies and for epigenetic research projects. For such research, it is essential that the materials and the biological data they contain are linked to **donors' personal data** or that they can be so linked (e.g. by consulting the attending physician or the patient in question). This includes demographic data (identity, age, sex) and background information on the donor (medical records, data on diet, lifestyle or local environmental factors). In addition, examples already exist of biobanks seeking to link their samples and data to data on benefits, earnings and employment, or on criminal convictions (Nuffield Council on Bioethics 2015, Sect. 7.15).

28 Such links between samples/biological data and donors' personal information make it possible for researchers to identify correlations between genotype and phenotype. To ensure that the linkage can be preserved over time, data is not irreversibly anonymised, but at most **pseudonymised**, i.e. assigned one or more codes (Nuffield Council on Bioethics 2015, Sect. 7.13).

Storage of samples and data

29 Substantial differences can also be observed with regard to the **period of storage** of samples and data. Biobank resources frequently remain available for future research projects either indefinitely (e.g. UK Biobank) or at least for an extended period (e.g. samples collected as part of a multi-decade cohort study). However, collections may also be designed to be maintained for a shorter period – e.g. for the duration of a specific research programme – and then liquidated or transferred to another biobank.

30 From a **technical viewpoint**, storage also varies. Biomaterials may be stored without processing, but it is not unusual for samples to be processed – e.g. blood may be centrifuged or DNA extracted from cells. In addition, samples may be stored either fixed (usually fixed in formaldehyde and embedded in paraffin) or "fresh", i.e. deep-frozen; in the former case, tissue and cell structures are better preserved, and in the latter, genetic and genetically encoded material (DNA, RNA, proteins). Data may be stored either on internal or external servers, especially in cloud storage systems (cf. Box 7); rather than setting up an internal database, connection to third-party databases is also possible.

31 In practice, there are also collections where what is stored is not samples as such, but information – e.g. on DNA – derived from samples (**analytical data**). If the analytical data obtained from biomaterials is associated with demographic and background data on donors, the database is also considered to be a biobank. An example is the openSNP database, founded in 2011 by German biotechnology researchers, where direct-to-consumer genetic test customers can publish their test results free of charge, together with phenotypic information (cf. Box 9).

Research involving samples and data

32 The relationship between a biobank and researchers can also take a variety of forms. Firstly, there is the **pure biobank**, which does not conduct research itself, but merely makes samples and data available to external research groups. This is typical of large-scale institutions such as the UK Biobank. Biobanks of this kind often have detailed regulations governing relationships with researchers (access, fees, handling of transferred samples and data, sharing of profits from commercially exploitable results, etc.).

33 Secondly, a research group or consortium may establish a collection of its own, so that it can carry out multiple projects in a specific field. Here, the biobank and researchers are part of the same organisation, and this can be described as a **researcher biobank**. This term is also applicable to cases where a pharmaceutical company uses its own collections of materials from clinical trials for further internal research projects. Mixed forms are also possible, e.g. if tissue samples stored in the archives of a hospital's pathology department are not only used for internal research but also transferred to third parties for research purposes.

Platforms and networks

34 From a research perspective, it is crucial that access to the samples and data stored in biobanks should be open and straightforward. To obtain statistically meaningful insights, the greatest possible quantities of samples and data are required. It is therefore important that biobanks should **collaborate** across national boundaries and ensure that data is made available in **standard formats**, so that it is comparable with data from other sources.

35 In practice, platforms and networks have been developed which provide researchers with information on the collections and data held by individual biobanks, facilitating access to and even interlinking such collections. Examples of **decentralised structures** at the European level are the Biobanking and BioMolecular resources Research Infrastructure (BBMRI) and EuroBioBank, a network of biobanks dedicated to rare disease research. At the national level, the Swiss Biobanking Platform – a project initiated in 2014 with support from the Swiss National Science Foundation – coordinates the activities of Swiss biobanks and collaborates with the BBMRI (Box 3).

2.2 Clarification of terminology

36 The concept of a biobank has been elucidated by the above description of the variety of biobanks existing in practice. A number of key terms are explained below:

- Biobanks are **collections of biological materials** (tissue samples, stem cells, body fluids such as blood, saliva, urine, etc.) from living or deceased persons in combination with **data** held in databases[6]. The data comprises demographic data (e.g. name, sex and age of donors) and background data (e.g. donors' medical records and personal circumstances). A biobank may store biological materials in a physical form (fixed or deep-frozen) or the analytical data obtained from the materials (i.e. data on biological characteristics of samples).

- Biobanks may transfer materials and data for various **purposes**, specifically for diagnostic and therapeutic purposes, or for research purposes, with the latter being broadly or narrowly defined. This Opinion only deals with **biobanks for research**, as these are associated with particular opportunities and risks. Biobanks for diagnostic and therapeutic purposes are not covered, unless the materials and data they hold are also made available for research.

- The **origins** of the materials and data stored in a biobank for research may vary: they may come from a diagnostic or therapeutic context, or have been obtained specifically for storage in a biobank. Also possible are the transfer of existing collections to (other) biobanks or the opening of existing collections for (further) research purposes.

- Typically, a biobank will store materials and data for use in future, as yet **unspecified research projects**. Biobanks are thus future-oriented and – as the term "bank" suggests – serve an intermediary function. The use of samples and data for research projects not specified at the time of donation gives rise to special normative challenges which do not arise within the traditional study participant-researcher relationship – e.g. the issue of general consent to future research with donated materials

6 Collections of biological materials of animal origin raise different problems and are not dealt with in this Opinion.

(marg. nos 92 ff.), or the question of mandatory authorisation for a biobank as such rather than for individual research projects (marg. nos 194 ff.).

– To a certain extent, however, whether collections are to be classified according to the intermediary-function criterion depends on how broadly or narrowly research projects are defined. For example, various research questions could be bundled into a single project in order to avoid a collection being classified as a biobank and subjected to the relevant data protection standards. The data protection standards applicable for biobanks should therefore also be applied to collections of samples and data established for a specific research project, e.g. as part of a clinical trial involving skin cancer patients. Whether such **project-related collections** are also called biobanks is not decisive from a normative viewpoint. What is essential is that such collections – where appropriate – are also governed by the standards applicable for biobanks. At the same time, smaller, low-risk research projects (e.g. for medical PhD theses) should be less tightly regulated.

– The materials and data held in biobanks are **generally pseudonymised**, i.e. they can only be traced back to specific persons via one or more codes (cf. marg. no. 122). However, materials and data may also be held in an identifiable (uncoded) or fully anonymised form.

3. Medical, social and ethical aspects

37 In the light of the key medical **facts**, this chapter explores the benefits (Sect. 3.1) and risks (Sect. 3.2) of biobanks and biobank-based research for donors, patients and other groups, and for society as a whole. The (potential) positive and negative impacts of biobanks are then considered in relation to fundamental ethical principles (Sect. 3.3) and thus made amenable to **evaluation**.

3.1 Benefits of biobanks

38 Biobanks have become an essential resource for **biomedical research**. At the centre of recent efforts is the question of the genetic causes of diseases such as cancer, diabetes or cardiac disorders (genetic epidemiology, cf. Hardy & Singleton 2009; Manolio 2010), as well as other phenotypic human traits. This type of research employs statistical methods and is dependent on genetic information and personal (especially clinical) data from a large number of individuals. Since about the mid-1990s, it has developed at a rapid pace, driven by technological advances in human genome sequencing and by the growing medical relevance – and decreasing costs – of genetic analyses (Kubisch 2014, p. 33). Here, there is every reason to speak of a paradigm shift in biomedical research.

Biobank-based research

39 Traditionally, genetic research projects have been confined to the **investigation of particular genes or genetic variants** (polymorphisms). Such studies are based on an initial hypothesis and concentrate on the analysis of specific, predefined sections of DNA. For this reason, they are not expected to yield any findings of genetic susceptibilities which were not being sought – so-called incidental findings. As an example of this type of research, studies of breast cancer genes and their mutations could be mentioned: well over 1000 different mutations have been identified in the BRCA1 gene since it was first cloned in 1994 (Kubisch 2014, p. 36).

40 Today, **genome-wide methods** are increasingly being used to gain new insights into the genetic basis of diseases (Kubisch 2014, p. 36). In so-called genome-wide association studies (GWAS; cf. Hardy & Singleton 2009; Manolio 2010; Krawczak 2014, p. 39), the whole genome is analysed – often without an initial hypothesis – in order to identify statistically robust associations between genetic variants and specific disorders. The detection of an association between genotype and phenotype requires comparison of DNA sequences from a large number of individuals with and without a particular disorder (Krawczak 2014, p. 39).

41 Genetic or genome-wide studies are also carried out to investigate the relationship between genetic factors and the response to drugs (as well as other external agents such as environmental substances or microorganisms). These are known as **pharmacogenetic** or **pharmacogenomic** studies (Brockmöller & Sehrt 2014, p. 62). One of the methods used in these studies involves assigning patients to groups with different genetic characteristics (stratification; cf. Giger et al. 2013) and investigating whether the effects of clinical interventions differ from one group to another. The aim of such research is to optimise the use of existing drugs and to develop new drugs tailored to patients' genetic make-up; this is known as **personalised medicine** (Eckhardt et al. 2014).

Stakeholders of biobanks

42 The benefits of biobanks thus consist primarily in enabling and facilitating biomedical research and in generating knowledge about genetic/biological causes of diseases and individual responses to drugs and other environmental factors. **Fundamental knowledge** of this kind has the potential to promote the development of new and improved treatment methods and more effective use of existing treatments (especially drugs). However, such research also holds out the promise of early detection of genetic susceptibility to – and prevention of – diseases.

43 The stakeholders of biobanks, apart from researchers, are thus not only **future patients** and individuals with genetic risks, but also physicians wishing to offer more effective diagnostic and therapeutic methods. Socially and economically, centres of research and

industry also stand to benefit. The effects on overall healthcare costs are uncertain: costs could conceivably be reduced as a result of more effective treatments or products (Rudin 2013, p. 95); conversely, however, biobank-based research could increase the costs of research, thus leading indirectly to higher healthcare costs (cf. marg. no. 10).

44 Whether and to what extent the indirect benefits of biobanks, beyond those for research, will be realised for individuals and society remains largely unclear. The potential of such research is indisputable, but expectations can be disappointed. Genome-wide association studies, for example, have so far failed to deliver the hoped-for benefits (Krawczak 2014, pp. 40 f.). In general, investments in biobanks can probably only be expected to pay off in the **long term**, over a period of decades.

Benefits for donors?

45 Biobanks for research thus contribute to science and, in the long term, to the development of new treatment methods and therapeutic products from which coming generations could benefit. This means that, if individuals donate their samples and data to a biobank, they do so primarily for altruistic reasons, particularly with the idea of helping future patients. Biobanks are not, however, essentially designed to provide **health benefits** for donors themselves. Such benefits may arise if donors are informed about clinically relevant findings discovered (intentionally or incidentally) in the course of research projects involving biomaterials and, thanks to this information, are able to receive appropriate medical treatment. It is also conceivable that, based on information about genetic factors associated with the development of disease, effective preventive measures could be taken (medical interventions or lifestyle modification).

46 Another possibility would be **commercial rewards** for donors, either in the form of direct remuneration for donation of samples and data to a biobank, or in the form of sharing of profits arising from commercially exploitable research results. In practice, such benefit sharing is certainly difficult to implement, since there is usually a long "production chain" leading from donation, through collection, storage and processing of materials, and research and development, to the marketing of a method or product, and numerous actors contributing various amounts of effort and innovation are involved. However, as shown by the example of the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization, benefit sharing can indeed work if appropriate institutions and procedures are established (cf. Nagoya Protocol 2010, Arts 5 ff.).

47 As regards biobanks, there are in practice examples of research consortia which offer donors **genetic tests free of charge** (e.g. Coriell Personalized Medicine Collaborative; Personal Genome Project). However, a legal right on the part of donors to a share of the profits arising from research conducted with donated material, or any (patented)

products derived therefrom, has not been recognised to date[7]. In this connection, mention should be made of an action brought before a court in Florida in 2000 – Greenberg v. Miami Children's Hospital Research Institute. The plaintiffs in the case were Daniel Greenberg and the Canavan Foundation, which had established a collection of samples and data known as the Canavan Registry (cf. Sect. 2.1.). Using this collection, researchers at Miami Children's Hospital isolated the gene responsible for Canavan disease (a neurodegenerative condition) and developed a genetic screening test. The hospital subsequently obtained a patent on the gene, forced the Canavan Foundation to stop offering free screening, and charged laboratories high licensing fees, so that access to the test was severely restricted. The case was settled out of court in 2003. Thereafter, the hospital was able to continue charging licensing fees and was not obliged to provide free access to the test for affected families; however, it agreed to allow licence-free use of the patented gene in research to cure Canavan disease[8].

3.2 Risks of biobanks

Risks to personal integrity

48 Research projects using samples and data from biobanks are so-called **retrospective studies**, which do not involve any interventions affecting the human body or mind; they are thus not deemed to be clinical trials (as defined in Art. 3 let. l HRA). Accordingly, such research does not involve any risks or burdens for individuals' physical or mental integrity. Interventions affecting integrity only occur in connection with the **sampling** of blood, tissue and other biomaterials for the purpose of storage in a biobank. The risks and burdens of such interventions are generally minimal; examples include the collection of saliva, urine or stool samples, peripheral blood sampling, swabs, or skin punch biopsies of limited extent (cf. Art. 7 para. 3 HRO). Often, because such samples are routinely collected for diagnostic or therapeutic purposes, no additional intervention is required for research.

Risks to privacy

49 The establishment and operation of biobanks does, however, affect donors' privacy in various respects. Privacy is affected in cases where biological material and personal data are **collected** for biobanks, or existing samples and data are **transferred** to or **stored** in biobanks. Privacy is, however, only affected if the material and data are directly identifiable or can at least be linked to the donor via a code (pseudonymisation). If the material and data have been irreversibly anonymised and the link to donors is thus destroyed, risks to privacy are excluded. However, whether irreversible anonymisation – especially of genetic data – is in fact possible is increasingly being questioned (see marg. no. 51

7 Cf. US court decisions in re Moore v. Regents of the University of California, 1991; Greenberg v. Miami Children's Hospital Research Institute, 2003; Washington University v. Catalona, 2007.

8 Canavan Foundation and Miami Children's Hospital joint press release, 2003.

for a discussion of re-identification of anonymised samples and data). Irrespective of this point, samples and data stored in biobanks are not generally anonymised, but pseudonymised (cf. marg. no. 28).

50 In practice, biobanks transfer pseudonymised samples and data to researchers without providing access to the key. From the researchers' viewpoint, the samples and data are thus anonymised. To this extent, privacy is not (additionally) affected by the **transfer** of samples and data from biobanks to researchers and the **further use** of samples and data for research. The situation differs in the case of researcher biobanks, where the researchers are also the owners of the sample and data collection (cf. marg. no. 33). In such cases, there are greater risks to privacy if the researchers have access to the key or the samples and data have not yet been pseudonymised. Risks arise in particular from the fact that research on samples and data may generate new knowledge about the donors concerned, e.g. regarding genetic susceptibility to serious diseases, or clinically relevant findings. This is sensitive personal information which – if the individuals concerned are identifiable (possibly via a key) – must not be disclosed to third parties without their consent.

51 It should also be borne in mind that even anonymised samples and data can possibly – with a certain amount of effort – be **re-identified**. Anonymised genetic data in particular can be linked to the person concerned if it can be compared with existing – non-anonymised – reference data, e.g. in the databases of police authorities and intelligence agencies or even private companies (Bohannon 2013; Nature 2013; Nuffield Council on Bioethics 2015, Sects 4.14 f). Re-identification may, however, also be relatively straightforward with the aid of general biographical details such as region, ethnic origin and occupation, if this information is compared with publicly accessible (e.g. online) data.

52 Because it relates to health and (possibly) other personal or social characteristics, the information stored in biobanks is **highly sensitive personal data**. It is vitally important that such data should remain exclusively within the research setting and not be disclosed to third parties (insurers, employers, etc.) without the consent of the persons concerned, or misused for purposes not related to research. Abuses may occur, for example, if biobank data storage is not sufficiently secure, coding is inadequate, or data is sold to third parties by biobanks or researchers. A serious – though possibly justifiable – infringement of privacy also occurs when biobank data is accessed by criminal justice authorities.

53 It is also conceivable that the privacy of donors may be compromised if – without being consulted or against their wishes – they are informed about genetic susceptibilities to serious diseases, clinically relevant findings or other personally relevant results discovered in research projects. Donors' relatives may also be indirectly affected if they learn

about a genetic risk existing within the family. What is at stake in such cases is people's right not to have to live with an awareness of distressing information concerning themselves and their health (**right not to know**).

Risks of discrimination

54 In **research ethics**, risks of discrimination are associated with the disproportionate involvement of particular groups in research projects (e.g. patients in developing countries, African-Americans in the Tuskegee Syphilis Study) or with the exclusion of groups (e.g. women, children, patients with rare diseases) from projects. A further danger of discrimination arising from genetic research in general lies in the fact that insurers could increasingly assess disease risks on the basis of genotype-phenotype correlations and select risks accordingly.

55 Also in connection with biobanks, risks of discrimination cannot be automatically ruled out. Although biobanks tend to offer additional sections of the population and patient groups the opportunity to be involved in research, frequently only institutions of a certain **size** and with substantial **financial resources** – such as university and central hospitals – can afford to develop biobanks and involve their patients in research of this kind. In contrast, smaller regional hospitals and primary care practices do not generally have the personnel or financial resources required to establish their own research infrastructure or to engage in collaborative projects. Such services are not reimbursed by health insurers. Patients who do not undergo treatment at larger hospitals are thus excluded from biomedical research (cf. marg. no. 7). Apart from such discriminatory effects, this may lead to bias in research results. For this reason, Nordic countries, for example, seek to ensure that patients of all types are invited to donate samples and data for research. Whether such an inclusive approach can be successfully implemented is ultimately also a question of financing.

56 Similar risks could arise if biobank research tended to focus on **more highly educated sections of the population**; this could be the case if interactions between donors and biobanks become increasingly complex as a result of elaborate rights of informed consent and withdrawal.

57 Discrimination would also occur if biobanks were established for **subgroups** in the absence of legitimate – i.e. research-related – reasons, e.g. for prisoners or young offenders, but also in relation to specific genetic variations.

3.3 Ethical principles

58 The above-mentioned opportunities and hopes associated with – and risks posed by – biobanks are reflected in the classical ethical principles articulated by Beauchamp and Childress in the late 1970s – autonomy, non-maleficence, beneficence and justice (Beauchamp & Childress 2012). Also of relevance to biobanks are the principles of solidarity,

participation and trust. To a certain extent, these ethical principles are also recognised in constitutional law in the form of basic rights and legal principles, and as public interests. The various principles are relevant to biobanks to varying degrees. With regard to specific issues and problems (e.g. data protection, commercialisation of biobanks, communication of research results to donors), the principles concerned are to be **weighed against each another**. Below, the benefits and risks of biobanks are considered in a general way in relation to the principles in question.

Autonomy

59 Autonomy is a fundamental characteristic underlying human **dignity and personality**. The right to autonomy means that voluntary, conscious decision-making is to be respected as the only legitimate determinant of a person's actions. The person must be able to act freely, unimpeded by internal (cognitive or emotional deficits impairing capacity) or external obstacles (threats, pressures, lack of relevant information, etc.).

60 The right to autonomy and respect for the patient's wishes is a central principle of bioethics. In Swiss law, the right to autonomy with regard to interventions of any kind affecting physical and mental integrity is derived from the fundamental right to personal liberty (Art. 10 para. 2 Federal Constitution). The right to autonomy also encompasses the right to control the flow of personal information from the individual to third parties and vice versa. This so-called right to **informational self-determination** is part of the fundamental right to privacy (Art. 13 FC).

61 Current developments in the areas of genetic analysis and bioinformatics pose new kinds of challenges for the right to informational self-determination. By collecting and using samples and linking them to data, researchers can gain access to personal characteristics of donors which may previously have been inaccessible to the donors themselves. The persons concerned must therefore give their informed consent. However, as we have seen, biobanks store samples and personal data for future research projects which are not yet specified at the time consent is given (marg. no. 36). Thus, donors do not know exactly what their samples and data will be used for, and what information and findings can be obtained from them. For this reason, a new form of consent – **general consent** – is employed: donors consent to their samples and data being used for research in general, rather than for specific research projects. With this type of consent, they do not have to be consulted and informed anew before each project. Whether the resultant facilitation of research is compatible with the right to autonomy will be discussed below (marg. nos 92 ff.).

62 Another type of question concerns genetic tests which enable health risks to be identified long before any symptoms of disease appear. In particular, with the aid of preventive or presymptomatic genetic analysis, mutations can be detected which indicate a **predisposition to avoidable diseases** (Lazaro-Muñoz et al. 2015). In research projects,

as soon as genetic variants are identified which are associated with an increased risk of disease for which preventive or risk reduction measures are available (medically actionable genes, MAGs), the question arises whether these results are to be reported to the person (not yet patient) concerned. Essentially, the right to autonomy requires that information relevant to the conduct of a person's life should be communicated. However, it needs to be borne in mind that the interpretation of genetic data is highly complex and may involve substantial uncertainties (particularly in the case of variants of unknown/uncertain significance, VUS; cf. Moret, Hurst & Mauron 2015). In such cases, the right to autonomy of the persons concerned can only be safeguarded if they receive appropriate expert support and counselling in dealing with this information.

63 Largely unresolved, lastly, is the fundamental ontological question of the **relationship between a human being and his/her body** and the associated legal implications (cf. the overview in Karavas 2015, marg. nos 18 ff.): Does the use of biological materials involve consent (in the sense of exercising the right of self-determination over one's body), or merely authorisation (in the sense of granting authority to a representative), or the exercise of property rights (in the sense of rights of disposal over an object)? Is the right of self-determination a right to control the substance (biological material) or the information (genetic and other information derived from the material)? And: is genetic information (also) common property? Does genetic information belong to researchers when it is processed?

Non-maleficence

64 Non-maleficence ("do no harm") is a universal ethical requirement which protects the personal liberty and integrity of human beings. In connection with biobanks, the principle of non-maleficence is relevant in two respects: firstly, with regard to the collection of biomaterials, to the extent that this involves **interventions affecting physical integrity** (cf. marg. no. 48); secondly, with regard to the **impacts on privacy** associated with the donation of samples or the provision of personal data (cf. marg. nos 49 ff.).

65 While the physical damage resulting from the collection of biological material can be said to be relatively slight, more substantial challenges arise with regard to the protection of privacy. The mere knowledge that **third parties** are in possession of information concerning one's health, genetic susceptibility to disease, or other personal characteristics may represent a considerable burden. If such information ends up in the wrong hands and is used for unauthorised purposes, the persons concerned can be significantly harmed, for example if – because of the health problems or disease risks revealed – they are denied insurance coverage, lose their job or have to terminate a partnership.

66 Harm may also arise in cases where persons **have to live with the knowledge** that they have a significantly increased risk of developing an (incurable) disease. This concerns

genetic predispositions in particular. Genetic analyses which reveal a susceptibility to disease within or across individuals (e.g. within a family) increase the vulnerability of the persons concerned – who are not (yet) affected by the condition – by transporting them into a more or less remote, but bleak future. This can influence their present emotional state, causing mental anguish. Potential adverse consequences of this kind have been discussed in particular in connection with newborn and child screening programmes for cancer (Clayton et al. 2014). Awareness of a susceptibility to disease can give rise to anxiety, fatalism or a sense of loss of control in the children concerned (Hall et al. 2014), and parents may develop adverse behaviour patterns (e.g. overprotectiveness). Such burdens are not, however, an inevitable result of biobank-based research; they can be avoided if donors are given the option of not being informed about presymptomatic genetic test results, or if a biobank does not generally communicate such information to donors.

Beneficence

67 The bioethical principle of beneficence requires persons to promote the welfare of others, as far as this is possible and reasonable. As explained above, biobanks are not essentially designed to provide health benefits for sample donors (marg. no. 45). In contrast to the typical physician-patient relationship, donors act altruistically, and the role of a biobank is not to help donors. Nonetheless, researchers may possibly discover **incidental** health-related **findings**, and the question thus arises of how the **return** of such findings to patients is to be managed (Husedzinovic et al. 2015; Lazaro-Muñoz et al. 2015). In such situations, researchers face the difficult question of whether – though not acting in a therapeutic capacity – they have a duty of beneficence vis-à-vis the donors concerned and should – in their best interests – communicate the incidental findings to them, perhaps even without the donors having consented in advance to receive such information (Elger & de Clercq 2015).

68 In its guidelines for the reporting of incidental findings (Green et al. 2013) – subsequently updated in response to various criticisms (Shaw 2015) – the American College of Medical Genetics and Genomics (ACMG) recommended that "unexpected" findings concerning (likely) pathogenic alterations in genes should be reported – whether patients wish to be informed or not. In such a case, the **patient's best interests are defined by third parties**, which runs fundamentally counter to autonomy and privacy rights. Some authors, however, take the view that this paternalistic approach is justifiable because of the asymmetry of knowledge between the health professional and the patient, with the former having a moral duty to do good (beneficence) and prevent harm (non-maleficence). Moreover, it is pointed out that a process respecting informed consent and involving extensive genetic counselling would require considerable resources (time, personnel, etc.), would be difficult to manage, and "might result in deeply varying levels of truly informed preference setting" (Green et al. 2013). Lastly, it has been argued that failing to respect the right not to know would actually enhance patient autonomy, by

providing "a fuller menu of worthwhile options" (Vayena & Tasioulas 2013). In contrast, other authors maintain that such duties of beneficence need to be weighed against the right to informational self-determination and the protection of privacy.

69 Weighing up duties of beneficence and autonomy and privacy rights becomes extremely difficult and complex when biobanks and researchers have to handle huge amounts of information, the interpretation and clinical relevance of which involves major **uncertainties** (cf. marg. no. 62). Further complicating matters is the fact that genetic information can also affect the patient or donor's **family members**, who have not consented to participate in the research. As genetic information is, of its nature, transindividual, it may reveal risks for relatives which they not only do not wish to know about, but whose psychological and existential impacts may be very hard to bear. In such situations, the tensions are exacerbated between the principle of beneficence on the one hand, and that of non-maleficence and the right to autonomy, on the other.

Justice

70 Justice is a multifaceted ethical principle. Since Aristotle, a distinction has been drawn between distributive and rectificatory justice (Höffe 2015, pp. 23 f.). In connection with biobanks, firstly, **questions of distributive justice** arise: who benefits from them, and from biobank-based research? Do biobanks involve risks of discrimination for certain groups (marg. nos 55 ff.)? Overall, do biobanks increase the costs of research, thus also leading to increased healthcare costs?

71 Biobanks for research have only recently become widespread. Accordingly, experience with biobanks remains limited, and the associated **societal impacts** are difficult to predict. In addition, as noted above, a wide variety of biobanks exist, and there are major differences from one country to another (cf. marg. nos 18 ff.). Consequently, the questions raised concerning distributive justice can scarcely be answered at present. It is important, however, that civil society should be aware of these issues and also monitor the future development of biobank-based research from the perspective of distributive justice.

72 Considerations of distributive justice do, however, demand that the **research results** obtained with the aid of donated biological materials and data should be **published** and thus made available to other researchers and the public. It would be unacceptable if, rather than benefiting the scientific community as a whole, the voluntary contributions to research made by numerous donors yielded results that were "privatised" for the benefit of a handful of researchers.

73 As well as distributive justice, questions of **rectificatory justice** arise in connection with biobanks. The central question is the sharing – with donors and biobanks – of profits arising from products derived from research on altruistically donated samples. Apart

from the practical question of whether and how such benefit sharing could be implemented (cf. marg. no. 46), the fundamental – normative – question arises of whether justice requires that profits generated by research and industry should be shared with donors or biobanks. If donors voluntarily contribute samples and data in the knowledge that they will not be (financially) compensated, this amounts to a kind of gift which cannot give rise to a moral or legal obligation to provide compensation. From this perspective, a benefit sharing obligation can only be based on contractual agreements to this effect between the parties concerned.

74 Here, the further question arises of whether the state has a duty to take **measures** to enable and promote benefit sharing agreements. Such measures would have to involve, firstly, the removal of obstacles, specifically the lifting of the prohibition on commercialisation of biological materials (marg. nos 154 ff.). Secondly, it is conceivable that the state – as envisaged in the Nagoya Protocol, for example (marg. no. 46) – could establish institutions and procedures to facilitate effective implementation of benefit sharing.

Solidarity

75 Solidarity has been historically and continues to be – e.g. in relation to bioethical questions concerning biobanks – understood in quite different ways (Bayertz 1998; Prainsack & Buyx 2011). An element featuring in most conceptions of solidarity is the idea of **people coming together and taking collective action to jointly attain a goal** which could not (or not as effectively) be achieved individually. Various other ideas are frequently associated with the concept of solidarity: firstly, the appeal to a shared identity based, for example, on nationality, poverty, powerlessness, occupation, gender or religion, or a genetic characteristic which leads people to see each other as equals – at least in this respect. Another frequently important aspect of solidarity is that, transcending the immediate interpersonal level, it involves the institutional and systemic level – e.g. in the establishment of social welfare systems.

76 Solidarity is sometimes understood in a purely **descriptive**, but often in a **prescriptive sense**, namely as a moral principle. In Catholic social ethics and also in recent bioethical discourse, solidarity is conceived – as a kind of bridging principle – both descriptively and prescriptively (i.e. imposing moral demands). The idea is that, because humans are relational beings, they should also support each other and solve problems jointly; as relational beings, it is argued, humans cannot be indifferent if some of their number are directly or systematically disadvantaged. The *descriptive* account alludes to the idea that, from a natural viewpoint, all humans are the same and interdependent (cf. also marg. nos 82 f. for the notion of "scientific citizenship", a social perspective), and that in a certain sense solidarity can be understood as a principle for the construction of a just society. In the *prescriptive* account, it is then a moral demand that people should pro-

vide mutual support and that, in addition, the institutions required to facilitate solidarity should be created within a society (cf. Machado & Silva 2015).

77 In the Preamble to the Swiss Federal Constitution, the idea of solidarity is implicit, for example, in the statement that the strength of a people is measured by the well-being of its weakest members. Related to the solidarity principle are not only the principles of responsibility, beneficence, dignity, reciprocity, participation, trust and the common good but also the demand for altruistic behaviour (Prainsack & Buyx 2011; marg. nos 71 and 74 ff., 83, 85 ff., 108 ff.). Frequently, as again in contemporary communitarian and bioethical discourse, the principle of solidarity is seen as a **counterweight to an overemphasis on the principle of autonomy** and individual freedom.

78 Of prime importance in connection with biobanks is the idea that people **generally make their samples available for research free of charge**, although in the vast majority of cases they cannot expect to benefit individually (marg. no. 45). People donate their biological material for research out of solidarity, in order to make a contribution to public health and the welfare of future patients, and not because they hope to benefit personally. Commercialisation of donations, in the form of direct compensation, would most probably lead to a decline in readiness to donate for reasons of solidarity (marg. no. 107).

79 It would be ethically problematic to assume that, given people's readiness to express their solidarity on the basis of a voluntary, autonomous and informed decision, a similar readiness can also be taken for granted in **persons who lack capacity**, e.g. in infants, children and patients with dementia (marg. nos 110 ff.). Appeals to the principles of solidarity and the common good must not result in the more fundamental personal autonomy and protection of particularly vulnerable persons being called into question. Voluntariness is essential to an appropriate conception of solidarity, and "compulsory solidarity" or a presumption of readiness to donate on the part of persons lacking capacity could not be ethically justified. Moreover, in the medium to long term, coercion of any kind would seriously jeopardise both trust and readiness to consent.

80 A special situation arises when persons who are affected, for example, by a **rare disease** come together nationally or globally to establish or support a biobank (marg. nos 21 and 188, but cf. also marg. no. 46). In this special case, donors and biobank operators may represent shared – possibly also commercial – interests, which is to be welcomed from an ethical viewpoint in accordance with the solidarity principle. Commercialisation of biobanks is not in itself antithetical to solidarity – in principle, the voluntariness of donations is not affected (marg. nos 185 ff., cf. also Box 11: even in the case of a for-profit organisation such as 23andMe, a large majority of customers are prepared to make their data available for research purposes free of charge). Here, too, however, it

needs to be ensured that the voluntary consent of those concerned is not compromised by subtle pressures.

Participation

81 The involvement of citizens in decision-making processes – in all areas, not just healthcare – is generally regarded in political philosophy as a regulative ideal. Free deliberation and the search for the best argument allow citizens, society or a nation to legitimize collective decision-making and resultant legal norms. As emphasised by the authors of the WHO report "Priority Medicines for Europe and the World" (Kaplan et al. 2013), the ideals of **legitimacy**, **transparency** and **accountability** are vital elements of free political debate and thus an essential part of any democratic society.

82 The readiness to involve patients, the insured, research subjects and donors in healthcare decision-making processes is a relatively recent phenomenon. Such participatory approaches make it possible to take the values and interests of interested parties into consideration in technology assessments and health policy decisions (Council of Europe 2000). Some authors see this as an attempt to go beyond the boundaries of representative democracy so as to attain a deliberative democracy, in which decisions are taken to a greater extent on the basis of a public exchange of rational arguments and the involvement of *all* interested parties, including interest groups such as citizens' associations (cf. Steiner 2012; Elster 1998). Accordingly, in relation to biobanks, the idea has emerged of a type of governance which includes donors and broad sections of the public, and which is intended to overcome the limitations of legitimacy based on individual informed consent. Complementing the personal and confidential perspective of the consenting patient or donor, various authors have argued for the development of a kind of social participation which could take the form of **scientific citizenship** (Weldon 2004). But however compelling such an approach may appear to be in general terms, its practical implementation appears to be no less difficult and controversial.

83 Empirical studies have shown that, while the involvement of patients and the public is recognised as a component of the deliberative process promoting open dialogue and shared decision-making, different views are taken of the value to be assigned to such elements (Rise et al. 2013). In addition, the terms "public" and "involvement" are understood in different ways (Sénécal, Stanton-Jean & Avard 2013): does the **public** ideally comprise all those directly or indirectly affected by a decision or only a limited subset, selected for example from interest groups or randomly from the population as a whole? Does **involvement** mean a consultation whose results may also be ignored or sidestepped, or is it an indispensable condition for the validity of decisions?

Trust

84 As data, information and knowledge resources, biobanks not only offer benefits and opportunities (marg. nos 38 ff.), they also involve risks (marg. nos 48 ff.), which essen-

tially always arise when personal matters are handed over to or fall into the hands of third parties. While responsible management of sensitive information, guided by stringent legal standards, is considered a prerequisite, it is not in itself sufficient to motivate patients or healthy subjects to make their genetic material or health-related data available. Rather, what is crucial is their **trust in the responsible and careful handling** of their donated material and data.

85 The organisation of biobanks is confronted with an age-old problem: "There is no *complete* answer to the old question: 'who will guard the guardians?'" (O'Neill [2002, p. 6)]. Trust does not solve this problem, but is a response to its fundamental insolubility. Since the risk of misuse of data and information cannot be wholly eliminated – i.e. since **complete control** is **impossible** – the only alternatives are either to refuse to contribute, or to trust the institution's organisation and procedures. In the latter case, the risk of misuse is precisely not eliminated, but accepted for the sake of the advantages expected to arise from the controlled transfer of samples and information for research.

86 Trust involves an attitude of favourable expectation, adopted against one's better judgement or in the knowledge that future events are unpredictable. The reasons for the **granting of trust** remain – as it relates to future actions – inevitably ill-defined, but are essentially based on the reliability, credibility and integrity of the counterparty, the trustworthiness of the latter's aims and intentions. That the materials entrusted to biobank operators will be managed in accordance with the regulations, and that the institutional, legal and political mechanisms are effective – these points must be assumed. Whether these assumptions are in fact appropriate can only be judged on the basis of past experience. Extrapolating this into the future involves – like any action – an element of risk.

87 Biobanks are dependent on the granting of trust by donors, which in turn depends on the expected trustworthiness of the biobank's (future) operations. In contrast to close interpersonal relationships, where trust is fundamental and taken for granted, **institutional trust relationships** are characterised by anonymity and a lack of transparency. Someone who donates tissue or personal data to a biobank is trusting, not a specific person, but the institution, its organisation and procedures, its control mechanisms and the legal framework within which it operates. Personal trust is replaced by trust in a system. The latter is based on rules and norms, on their legal foundations, and on institutionalised procedures to control their application. Trust is placed in the system's established operating routines, and readiness to donate depends crucially on whether people's expectations concerning the functioning of the system are confirmed in practice, i.e. on whether the system is perceived as trustworthy.

88 However, trust is also involved in another – often overlooked – respect. Trust in the system is a prerequisite not only on the input side, but also on the output side. If biobank

materials and data are to be used for research, it must be guaranteed that collection, processing, storage, etc. meet scientific standards. As biobank stocks are normally generated long before they are used, researchers need to be confident that the biobank resources satisfy their own scientific requirements. For this, it is not sufficient that a biobank's procedures should be transparent; users must be able to rely on the procedures being carefully and comprehensively applied with regard to the resources in question. In turn, the **trust placed in the biobank by researchers**, as a prerequisite for using its resources, is a compelling reason for donors to risk entrusting their samples and data to the biobank.

4. Relationship between donors and biobanks

4.1 Information and consent

89 Respect for the autonomy of patients and persons participating in research projects is – as discussed above (marg. nos 59 ff.) – a fundamental principle of bioethics. From the autonomy principle, it follows that subjects can only be included in a study if, after being appropriately informed, they have given their voluntary consent. The requirement of informed consent also derives from the Constitution and from the protection of privacy under civil and criminal law. Of relevance in the case of retrospective studies involving biological materials and personal data is the privacy-based **right to informational self-determination**, i.e. the right to control the processing of information about one's own person.

Actions requiring consent

90 The **collection of samples** for storage in a biobank affects the integrity of the persons concerned and involves certain – albeit usually minimal – risks and burdens (marg. no. 48). Accordingly, voluntary informed consent is required.

91 The subjects' consent is also required if their **data is collected for biobanks** or if previously collected data is **transferred** to biobanks. The same applies to the transfer of samples already collected (for other purposes) to biobanks, as these materials are also carriers of (genetic and other biological) data. The requirement for informed consent stems from the fact that the data stored in biobanks – unless it is fully anonymised – is particularly sensitive personal data. Misuse of such data can cause substantial harm to the donors concerned (marg. no. 52). In view of the risks of misuse, it is essential that individuals provide voluntary informed consent for their samples and data to be stored in biobanks and made available for research. Consent implies a risk/benefit assessment, which calls for an autonomous decision on the part of the donor.

General consent

92 Questions arise with regard to the scope of informed consent. The fundamental problem is that, for a biobank to function, donors' consent to future, **as yet unspecified actions** is required. Firstly, biobanks have an interest in being able to update information on donors, particularly with regard to their medical history. For this to be possible, consent must also cover future disclosure and processing of personal data. Secondly, when samples are donated and data is transferred to a biobank, it is not yet known for what specific research projects the samples and data will be used in the future (marg. no. 36).

93 The question of the scope of informed consent to the use of biomaterials for research has been widely debated by ethicists and legal scholars (cf., for example, Haga & Beskow 2008). One approach commonly advocated is known as **general consent** (cf. marg. no. 61). Here, donors consent to the use of their materials and data for future, as yet unspecified research projects (for current legal regulations, see marg. nos 138 ff.). Consent is thus given to use for research *purposes*, rather than for specific research projects. General consent has been criticised because – contrary to the protection of privacy and to the principle of specificity in data protection law – it requires people to commit themselves for an indefinite period and for unspecified purposes (Büchler & Dörr 2008, pp. 402 f.).

94 How general consent is to be ethically evaluated must depend on whether and to what extent individuals can assess the risks and benefits of donation at the time consent is granted. The impact on privacy must be **sufficiently well defined at the time the donation is made**, i.e. donors must know what they are agreeing to. If, as a result of subsequent activities or events, significant changes occur with regard to the risks and benefits of the use of samples and data for research, renewed consent is required from the persons concerned.

95 As regards the **risks**, it would appear to be essentially sufficient if information is provided on the biobank as an institution, in particular on its purpose and organisation, and on the arrangements for the storage of materials and data. This is the case provided that the samples and data are transferred to external researchers in an anonymised form and they do not have access to the key, or the samples and data are used exclusively by internal researchers (researcher biobank, cf. marg. no. 33). In addition, appropriate measures are to be taken to ensure that the researchers do not attempt to re-identify the transferred samples and data (marg. no. 180). Under these conditions, no additional risks are created by the updating of donors' health-related data and the transfer of samples and data to researchers. This is because the risks depend on the security measures taken by the biobank, rather than on the type of research projects in which further use is made of the samples and data.

96 In contrast, the **benefits** will depend entirely on the research projects for which samples and data are made available by the biobank. The overall benefit of the donated samples and associated data corresponds, hypothetically, to the scientific value and practical relevance of all the research projects for which the samples in question are used. This overall benefit cannot possibly be defined in concrete terms, but only described in a highly abstract way, by indicating the research fields or types of research projects for which a biobank is designed (e.g. biomedical research or cancer research). In addition, the benefits of a biobank depend on what criteria are used and what bodies are responsible (e.g. scientific advisory boards or independent ethics committees) for the selection of research projects. To enable prospective donors to assess the potential benefits, they should therefore be informed about the type of research projects supported (purpose of the biobank) and the procedure for the selection of projects.

97 Thus, if samples and data are transferred to external researchers in an anonymised form, or the institution in question is a researcher biobank, **provision of information on the biobank as an institution** is sufficient to allow donors to assess and weigh up the risks and benefits of donation. Consent to each individual updating of health-related data or to each individual research project is not needed to preserve donors' right to self-determination. This is because, under the conditions specified, the risks and benefits of donation depend on the institutional design of the biobank and its research infrastructure operations – not on the particular research project in which samples are used.

Tiered consent

98 An approach discussed in the literature as an alternative to general consent is that of tiered consent (Haga & Beskow 2008, p. 520). Here, having been informed about the biobank's organisation and activities, donors are given the option of excluding certain kinds of use (e.g. certain types of research projects, profit-oriented research, transfer of materials and data to other biobanks or abroad). Tiered consent is designed to protect donors' self-determination rights more effectively than general consent. While biobanks are free to adopt approaches of this kind, a requirement to offer tiered consent would go too far: firstly, donors' autonomy can also be adequately safeguarded by means of general consent (marg. nos 94 ff.); secondly, the implementation and administration of tiered consent for large numbers of people may prove to be **highly time-consuming and complex**. Accordingly, if tiered consent were to be imposed by the state, excessive obstacles to the establishment and operation of biobanks for research would be created with no compelling justification.

Revocation of consent

99 Even though individuals are informed about the risks and benefits of donation when they donate their biomaterials, it must be possible for them to withdraw at any time. Committing oneself for an indefinite period would be excessive and difficult to recon-

cile with the right to self-determination. Donors must therefore have the **right to revoke their consent at any time** without being required to give a reason. Withdrawal can take various forms: the donor's samples and data can be destroyed, or they can be merely anonymised and continue to be used – though without further updating – for research purposes. In the former case, the donor's samples and data, together with the code, are to be destroyed; in the latter case, only the identifying code is to be removed. It may be that complete elimination of all samples and data is not possible, particularly because sample components and data already transferred to researchers cannot be recalled or destroyed (cf. Nuffield Council on Bioethics 2015, Sect. 7.9). At the time consent is given, donors are to be informed that, even if it is subsequently revoked, their donation and its consequences cannot be fully reversed.

100 Donors expect their samples and data to be used in accordance with the purpose of the biobank for high-quality scientific research projects, thus generating benefits for society. It must be possible for them to assess whether these expectations are subsequently fulfilled. This means that donors must be informed about the biobank's activities and – if these do not live up to their expectations – they must be able to revoke their consent. Donors' right to self-determination thus demands **transparency**. Biobanks should provide at least general information about their activities, i.e. about the research projects supported and important organisational changes or appointments (e.g. amendments to by-laws or changes in management).

Transfers and changes of purpose

101 A biobank can be expanded and made more attractive for research if samples and data are acquired from other biobanks, or if one biobank is wholly integrated into another. It is also possible that a biobank will be liquidated because of insolvency or for other reasons and its stocks transferred to other biobanks. **Transfers of samples and data** may take place across national boundaries, worldwide. As we have seen, the risks and benefits of biomaterial donation depend on the biobank's purpose, organisation and operations, including its data protection measures and distribution policy vis-à-vis researchers. These factors can change significantly if samples and data are transferred to another biobank, either in an identifying form or pseudonymised (together with the key). Consequently, transfers of materials to another biobank in Switzerland or abroad will generally require the informed consent of the donors concerned.

102 The same applies to a **change of purpose** of a biobank, or any other substantial change significantly affecting the risks and benefits of donation. For example, if a biobank intends to make its samples available to the food industry for commercially oriented studies, donors' consent is to be obtained.

103 A special case of a change of purpose would be where a collection originally established for diagnostic or therapeutic purposes is made accessible for research (**reorien-**

tation). Examples include tissue collections of pathology institutes or blood stem cell banks (marg. no. 25). If, as a result of reorientation, samples and data are transferred to third parties for research projects, additional risks to privacy may arise; to be considered in particular is the risk of samples being re-identified and used by third parties for unauthorised purposes (marg. no. 51). For this reason, such reorientations will also generally require the informed consent of the donors concerned.

4.2 Voluntariness of consent

104 A key element of the autonomy principle is the voluntary nature of individual decisions. Voluntariness implies the absence of (negative) factors such as force, threats or deception, but also of (positive) inducements offered by third parties, which influence the person concerned to such an extent that **the pros and cons of a decision can no longer be freely weighed up** (cf. marg. no. 59).

Time of consent

105 As discussed above, if biomaterials and personal data are collected specifically for a biobank, informed consent is required in advance. More doubtful, however, is the question of when consent is to be obtained if tissue collected in connection with a diagnostic or therapeutic procedure (surgery) is to be transferred to a biobank. At the CHUV, for example, patients are asked after admission, but **before diagnostic or therapeutic measures are carried out**, whether they consent to the storage of samples and data in the Lausanne Institutional Biobank (BIL). The fact that they are facing medical treatment and are ready to display the greatest possible degree of cooperation in the interests of successful treatment may influence patients in their decision whether to donate samples for research.

106 Considerations of **practicability**, however, suggest that consent to the further use of samples for research purposes should be obtained before medical treatment. In addition, this can prevent patients – after what may have been burdensome therapies – from being confronted once again with their medical history as a result of enquiries from a biobank. It must however be ensured that the decision on donation of samples to a biobank is *freely* taken, i.e. that it does not affect subsequent medical treatment. In no way are patients even to be given the impression that their decision could have a favourable or adverse influence on their treatment.

Financial incentives

107 The free decision of potential donors could also be compromised by excessive financial incentives. In view of the risks and burdens associated with donation, however, **appropriate compensation** for donated materials could also be interpreted as an expression of rectificatory justice. At the same time, an argument against the commercialisation of biomaterial donation is the fact that readiness to donate declines if donors are paid. The conviction that one is doing good through an act of altruism and solidarity may be

undermined by payment. The so-called crowding-out effect of monetary compensation has been demonstrated in various empirical studies (cf. Mellstrom & Johannesson 2008; Niza et al. 2013).

108 Somewhat different to direct compensation for donors would be **sharing of the benefits arising from commercially exploitable research results**. This could take the form of a financial stake in the profits generated by research, or facilitated (e.g. free of charge) access to the methods and treatments developed. The latter in particular could not be construed as unethical commercialisation, undermining donors' autonomous decision, nor would facilitated access of this kind be expected to adversely affect readiness to donate. On the contrary, patients affected by a particular disease will (also) be motivated to donate by the prospect of new diagnostic and treatment methods being developed from which they and their relatives can fully benefit.

109 Accordingly, the **Universal Declaration on Bioethics and Human Rights** adopted by **UNESCO** on 19 October 2005 (UNESCO 2005) calls (in Art. 15) for the sharing of benefits resulting from scientific research. Among the forms which such benefits may take, the following are specified: (a) special and sustainable assistance to, and acknowledgement of, the persons and groups that have taken part in the research; (b) access to quality health care; (c) provision of new diagnostic and therapeutic modalities or products stemming from research; (d) support for health services; and (e) access to scientific and technological knowledge. At the same time, Art. 15 para. 2 of the Declaration explicitly states that benefits should not constitute improper inducements to participate in research. Article 15 was the subject of a report on the sharing of benefits published by the International Bioethics Committee (IBC) on 2 October 2015 (UNESCO 2015).

4.3 Special categories of donors

110 Biobanks also handle samples from donors who, because they lack capacity or for other reasons, cannot give voluntary informed consent to donate. These include children and adults who lack capacity (e.g. patients with dementia), embryos and foetuses, and deceased persons. In research ethics, and in the human research legislation (cf. Arts 21 ff. HRA), persons lacking capacity and embryos and foetuses *in vivo* are classified as **particularly vulnerable persons**. In Swiss law, this category also includes children or adolescents with capacity and prisoners. With regard to the donation of samples and data for biobanks, questions arise particularly in relation to children lacking capacity and the unborn, as well as deceased persons; these questions are discussed below.

Children and the unborn

111 For research involving biological materials, samples from **children** – especially newborns – are a valuable resource (e.g. cord blood banks or samples from newborn screening programmes). Such possible uses raise the question of whether samples and data from persons lacking capacity should be made available for research purposes at all.

112 If samples from persons lacking capacity are to be donated to a biobank, informed consent is always required from the legal representative, i.e. the parents or a deputy. In this context, however, proxy consent on behalf of persons lacking capacity is problematic insofar as the donation is not expected to provide any **direct health benefits**, but is to be considered as an act purely for the benefit of third parties (cf. marg. no. 45). At the national and international level, it is agreed in principle that such acts are permissible as long as they entail only **minimal risks and burdens** for the persons concerned who lack capacity; in the research sector, there is the additional requirement that a benefit is to be expected for the group concerned over the long term (so-called group benefit). These restrictions on non-therapeutic interventions in persons lacking consent also underlie the relevant Swiss legislation (cf. Arts 22 ff. HRA; Art. 10 para. 3 let. b and Art. 13 para. 2 let. a TransA; Art. 10 para. 2 HGTA), and views to this effect have also been expressed by the Commission (NEK-CNE 2009, pp. 12, 22 ff.).

113 The collection of samples for research purposes generally involves no more than minimal risks and burdens. If the samples are collected for diagnostic or therapeutic purposes anyway – which will usually be the case in children – research use does not entail any additional intervention affecting the child's integrity. However, in the area of biobank research, the main concern is not risks to integrity, but risks of misuse of data (marg. nos 48 ff.). This risk is to be rated as minimal if the samples and data are **securely stored** and if the risk that they may be used outside the research context to the detriment of the persons concerned can be practically ruled out. Thus, what is crucial is that the biobank should have sufficient institutional safeguards in place to ensure data protection and data security. Whether this is the case would have to be checked by an independent inspection of the biobank.

114 It should be borne in mind that children whose samples are stored in a biobank and used for research purposes can only exercise their **right to revoke consent** after attaining capacity if they actually know that their samples are being stored. The question thus arises whether a duty to provide such information should be imposed on biobanks. Such a duty vis-à-vis thousands of donors would probably involve enormous costs and be almost impossible to implement. As an alternative, an entry on the insurance card of the children concerned might, for example, be contemplated; this would enable children subsequently attaining capacity to be informed about the donation and, if appropriate, to exercise their right to dissent.

115 Similar questions arise when genetic material from **embryos and foetuses** is stored in biobanks and made available for research. This could take the form of cells extracted for prenatal diagnosis – using an invasive method (amniocentesis, chorionic villus sampling) or non-invasive prenatal testing (NIPT) – together with the test results. Also possible, however, is the collection and storage of early embryonic cells deriving from preimplantation genetic diagnosis. The use of such samples from the unborn for research

purposes is of course also only permissible with the parents' informed consent. Here, too, it is of crucial importance that data protection and data security are assured. As in the case of samples from children, there is the additional problem that the right to dissent cannot be exercised if the persons concerned do not know about their donation. Accordingly, the parents have a responsibility to inform their children about the donation when they have reached an age at which they can exercise their rights themselves.

Deceased persons

116 Another question which arises is how samples and data from deceased persons should be handled. If the samples and data have been **collected during the donor's lifetime**, nothing initially changes as a result of the death of the person concerned. After the death, however, relatives could be indirectly affected – for example, if extracts from the deceased's medical records become known to the public (protection of the memory of the dead) or genetic data allows conclusions to be drawn about blood relatives' predisposition to disease. This suggests that relatives (i.e. partners and blood relatives) should be granted a right to revoke consent. Donors would then have a responsibility to inform their relatives about the donation, thus enabling them to exercise their right to revoke consent posthumously.

117 A question which needs to be considered is whether the **posthumous removal of samples** should require consent given by the person concerned during his/her lifetime or – after death – by the donor's relatives (extended consent system), or whether it should be sufficient that the person has not dissented during his/her lifetime and that the relatives do not dissent (extended dissent system). An argument in favour of the consent system is the fact that it more effectively safeguards the autonomy of donors and their relatives. In contrast, the dissent system is more responsive to the interests of research and public health. In support of this system, it could be argued that, unlike the removal of organs from deceased (brain-dead) persons, posthumous donation of materials for research does not involve any risks to integrity, but merely certain – rather minor – risks to the (posthumous) protection of the privacy of the person concerned and that of the relatives (for the current legal situation see marg. no. 157).

4.4 Data protection and data security

118 Assurance of the right to self-determination is not sufficient to protect the privacy of donors. In order to prevent misuse of donors' – highly sensitive – personal data, **institutional safeguards** are additionally required. These include pseudonymisation of data, independence from organisations with a non-research-related interest in the biobank's data, and careful storage of samples and data.

Pseudonymisation

119 An essential measure to ensure data protection is pseudonymisation (coding) of the biological materials and personal data stored in a biobank. With pseudonymisation, personal identifiers are replaced with a **code**, so that materials and data cannot be identified by persons who do not have access to the coding key. Also possible is double- or even triple-coding, where personal identifiers can only be recovered using two or three separately stored keys (cf. Haga & Beskow 2008). For persons lacking access to the key, the materials and data are thus anonymised; from their perspective, the data in question is therefore no longer *personal* data (cf. Art. 26 para. 1 HRO).

120 Pseudonymisation is primarily designed to prevent sensitive personal data from falling into the hands of third parties and being used for unauthorised purposes. However, in accordance with the principle of proportionality, even where it is being processed for legitimate purposes, access to personal data should be limited to as few people as possible. This goal can best be achieved if the persons working with samples and data – i.e. researchers – do not have access to the key. The key is therefore to be stored separately from the persons involved in a research project, as is explicitly required under current legislation (Art. 26 para. 2 HRO). **For researchers**, the samples and data should thus remain anonymous. Achieving the goals of biomedical research does not require any knowledge of the personal identifiers of the samples and data used.

121 It would, however, be disproportionate to demand that samples and data be **fully anonymised** via irreversible removal of personal identifiers. This would mean that it would no longer be possible for data to be updated, e.g. with new entries in medical records. Nor would revocation of consent by donors then be possible, although complete anonymisation would also largely eliminate risks to privacy (apart from the risk of re-identification of anonymised samples, cf. marg. no. 51). In addition, with complete anonymisation, any medically relevant findings could no longer be communicated to the donors (cf. marg. nos 126 ff.). Nonetheless, biobanks must have the option of fully anonymising their samples and data. In this case, before consent is given, or before samples and data are anonymised, donors are to be informed that, as a result of anonymisation, they can no longer exercise their right to revoke consent or their information rights. In addition, it should be pointed out to donors that, even today, the anonymity of samples and data cannot be absolutely guaranteed.

122 For a biobank, the pseudonymisation of all samples and data, e.g. the removal of personal identifiers from medical records, may be **costly and time-consuming**. This is true in particular for collections which are established in a diagnostic or therapeutic context and (also) used for research, such as the collections of hospital pathology institutes. For data protection, it is crucial that data from the biobank is not accessed by third parties in an identifying or (with a key) identifiable form. Within the biobank, on the other hand, the question of which and how many individuals can identify the materials and

data is one of proportionality. For this reason, it must be sufficient that the samples and data are pseudonymised within an appropriate period. Pseudonymisation is, however, mandatory at the latest when samples and data leave the biobank and are transferred to external research teams (Rudin 2013, p. 97); this does not preclude specific consent being given by the donor concerned to the transfer of identifiable samples for a particular research project.

Biobank independence

123 Also important for data protection is that biobanks should be **independent** – in terms of personnel and financing – of institutions that could misuse donors' personal information, especially **health insurers**. Examples already exist of biobanks financed by health insurance organisations[9]. Dependencies of this kind are to be avoided if for no other reason than that they could undermine public trust in biobanks and biomedical research.

Careful storage

124 In order to ensure data protection, continued compliance with **quality and security standards** for the storage of samples and data is essential. These standards are defined in various international guidelines (OECD 2009; ISBER 2012; WHO 2007). The Human Research Ordinance specifies, in particular, that unauthorised or accidental disclosure, alteration, deletion and copying of health-related personal data is to be prevented; that all processing operations which are essential to ensure traceability are to be documented; that the technical requirements for appropriate storage of biological materials are to be met; and that the resources required for storage of materials are to be made available (Art. 5 HRO).

125 Particular problems are raised by the use of **cloud storage** (cf. Box 7). The services of cloud storage providers are used by biobanks to allow huge amounts of data to be securely stored at relatively low cost[10]. Cloud storage generally means that data is transferred abroad and is subject to the host country's data protection regulations. Most cloud storage providers are based in the US, where the data may be accessible, in particular, to the National Security Agency (NSA). Thus, while cloud storage can improve efficiency and data security, it can also lead to a reduction in the level of data protection. Given the risk of re-identification, this is also true in cases where data is stored in a cloud system in a pseudonymised or anonymised form (cf. marg. no. 161).

9 E.g. Kaiser Permanente Research Program on Genes, Environment, and Health (RPGEH): http://www.dor.kaiser.org/external/DORExternal/rpgeh/index.aspx

10 E.g. International Cancer Genome Consortium Pan-Cancer Analysis of Whole Genomes (ICGC PCAWG); cf. Nuffield Council on Bioethics 2015, Box 7.4.

4.5 Communication of research results

126 Whether and to what extent the results of research projects involving samples and data should be communicated to donors or the public is a controversial issue. A distinction is to be drawn between – possibly incidental – medically relevant findings concerning diseases or specific genetic susceptibilities (**individualised results**) and the generalisable scientific results which researchers are aiming for (**aggregate results**).

Medically relevant findings

127 In research projects involving biological materials, evidence may come to light of **existing diseases** (e.g. a malignant tumour discovered during tissue analysis) or of genetic **susceptibilities** to specific diseases (e.g. a monogenic cause of amyotrophic lateral sclerosis discovered in a genome-wide association study, cf. marg. no. 40). The results obtained may have been deliberately sought, but they may also be secondary (incidental) findings.

128 In the ethics literature, communication of clinically relevant findings to research subjects – particularly the results of genetic studies – is a controversial issue (Hansson 2009; Haga & Beskow 2008). Arguing in favour of the disclosure of individualised research results is the **principle of beneficence**, according to which not only should individuals have their decisions respected and be protected from harm, but – as far as possible and reasonable – their welfare should be promoted (cf. marg. nos 67 ff.). Access to individualised results can enable donors to take medical measures in good time, so as to treat a newly detected disorder or, in the case of a predisposition, to take preventive action. The overall benefits for society, and trust in biobanks, can thus be increased. Empirical studies indicate that donors are interested in receiving as much information as possible on health-related findings of research (Husedzinovic et al. 2015).

129 Those who are opposed to the communication of individualised results argue that research is specifically designed to produce generalisable knowledge which benefits, not individuals, but society as a whole. Accordingly, donors should not expect to receive any therapeutic benefits (the so-called **therapeutic misconception**). The relationship between a biobank, or researchers, and donors is not one of care, like that between physician and patient. Communication of individual findings to donors thus runs counter to researchers' professional ethos, which is not to be confused with that of medical practitioners. In addition, the results of a single research project are not to be overinterpreted and may turn out to involve spurious correlations or non-replicable findings. It should also be borne in mind that, given the large amounts of materials studied, a duty to report individualised results would pose major (also financial) challenges for biobanks and researchers. For example, considerable costs would arise not only for the clinical tests required for the validation of results, but also for the organisational structures and staff training needed to ensure appropriate communication of findings.

130 For the above-mentioned reasons, the information reported to donors should be restricted, firstly, to **medically relevant findings** which are scientifically valid and considered to be at least provisionally confirmed. In addition, the results to be disclosed should have significant implications for the health of the individuals concerned, and effective therapeutic or preventive options should be available. Results should be communicated via the physician or hospital caring for the patients concerned. To ensure effective communication, cooperation is required between researchers, biobank and hospital/physician.

131 Secondly, to avoid additional efforts and costs, biobanks and researchers must be free – with donors' consent – to adopt a **general policy of not reporting** individualised results. Donors' right to be informed cannot be absolute; rather, their right to informational self-determination encompasses the autonomous decision to forgo the reporting of health-related findings. The fact that some people may decline to donate under such conditions will be taken into account by the biobank or researchers.

132 If the biobank and researchers are in fact prepared to inform donors about medically relevant findings, they must respect donors' **right not to know**. This means that, when donors are informed about the procedure, they are to be asked whether they consent to the reporting of health-related (possibly also incidental) findings. Like the right to know, the right not to know derives from the fundamental right to privacy (Art. 13 FC).

Scientific results

133 Individuals donate biological materials for research in order to make a contribution to public health and the welfare of future patients (marg. no. 78). Various studies have shown that participants are eager to be informed about the overall results of research. An appropriate way of enabling donors to find out whether and to what extent their contribution has been beneficial is to provide lay-friendly information on the results. For example, this could take the form of summaries of scientific results published on the biobank's website. In general, such a policy of **transparency** tends to promote public trust in biomedical research.

134 In addition, it would be in the interests of transparent and efficient research for projects involving samples and data from biobanks to be recorded in **public registries** (for mandatory registration of clinical trials, see Art. 56 HRA). This could help to prevent not only multiple studies of the same scientific topics, but also the suppression of unsuccessful projects or adverse results. Public registration of research projects is thus to be seen as an element of good governance for biobanks.

4.6 Need for regulation

135 The donation of samples for biobanks is governed by the **Human Research Act** (HRA) and the associated **Human Research Ordinance** (HRO); on a subsidiary basis, general

privacy and data protection legislation is also applicable. Human research law regulates the details of informed consent to the collection and further use of biological materials and health-related personal data for research. While these provisions are applicable, they are not specifically designed for biobanks. As a result, current law contains a certain amount of overregulation – but also regulatory gaps – with regard to the donation of samples for biobanks.

Collection of samples

136 Under Art. 16 HRA and Arts 6 ff. HRO, persons from whom biological material is sampled or health-related personal data is collected for research must be informed about the nature, purpose and duration of, and the procedure for, the **research project**. This means that the procurement of samples and data for research purposes is only permissible if the projects in question are already defined. For biobanks which make samples and data available for future, as yet unspecified studies, this is not the case. Current law thus prevents the donation of samples and data for storage in a biobank.

137 As defined by the HRA, the sampling of biological material and collection of health-related personal data for research constitutes **research involving persons**. Accordingly – as for all research involving persons within the scope of the HRA – provision of appropriate information about the specific research project is a legal requirement. This restriction of research freedom is not, however, necessary to protect donors' integrity (generally only marginally affected in such cases) or privacy. Rather, it should be sufficient that, apart from any possible physical risks associated with the intervention, donors are appropriately informed about the biobank as an institution and its activities; this will ensure that donors are aware of the potential benefits of their donation and the associated risks to privacy (marg. nos 94 ff.). The requirement that donors must always be informed about the specific research project before samples and data are collected is thus not justified. With this requirement, the collection of samples and data for biobanks is excluded for no compelling reason; the relevant provisions should therefore be amended.

Further use of pseudonymised samples

138 For the further use of existing biological materials and health-related personal data for research, **different rules for consent** are specified in Art. 32 and Art. 33 HRA. Here, according to Art. 24 let. c HRO, "further use for research" also covers the storage of samples or inclusion of data in a biobank.

139 For the use of biological materials and genetic data in coded (pseudonymised) form, general consent is sufficient (Art. 32 para. 2 HRA); for the use of non-genetic health-related data in coded form, it is even sufficient if the person concerned has been informed in advance about use for research purposes and has not dissented (Art. 33 para. 2 HRA). For non-health-related personal data (e.g. data on donors' lifestyle or family relationships), the research privilege accorded by data protection law applies: such data may

be processed for research as long as the results are published in such a way that data subjects cannot be identified (cf. Art. 13 para. 2 let. e FADP). In the rules for consent specified in Art. 32 and Art. 33 HRA, the **concept of general consent** has thus become established in Swiss law.

140 With the system of general consent, however, donors should also receive basic information about the purpose, organisation and activities of the biobank in question. In this connection, the relevant ordinance specifies that donors are to be informed about measures taken to protect the biological material and personal data, and in particular management of the key (Arts 28 ff. HRO). More specific information about the further use of material and data for biomedical research is given in a template issued by Swissethics (Swiss Ethics Committees on research involving humans)[11]. The **types of information** specified in the ordinance and the template ensure that the risks of donation can be adequately assessed by the persons concerned. According to the template, donors are also to be informed that they will not benefit financially from the results of research, and that there will not generally be any direct health benefits, but that donation represents a valuable contribution to biomedical research and may help to improve the treatment of future patients. In order to gain a better understanding of the benefits of donation, donors should additionally be informed about the activities of the biobank in question (cf. marg. nos 96 ff).

141 An unconvincing aspect of the legislation is the **differentiation between genetic and other health-related personal data**. In both cases, the data in question is highly sensitive. Donors' privacy can be jeopardised just as much – if not more so – if what falls into the wrong hands are medical records stored in biobanks, from which more intimate information may emerge than from a tissue or blood sample. The same applies, moreover, for non-health-related personal data concerning the donor, e.g. lifestyle data. It should be borne in mind that the storage of samples in combination with health-related and other personal data in biobanks facilitates the compilation of a personality profile, permitting the assessment of essential characteristics of an individual's personality (cf. Art. 3 let. d FADP). In view of the risk situation, it would therefore be appropriate, in the area of research, to move away from genetic exceptionalism of the kind applicable in the context of medical treatment (cf. Art. 119 para. 2 let. f FC and HGTA). Accordingly, a general consent requirement – and not merely a right of dissent – should be specified for the further use of all pseudonymised personal data.

11 Swissethics, Information on the further use of biological material and/or health-related data for biomedical research (Version V-2.0, 16.07.2014, biobanks), available at: www.swissethics.ch/doc/ab2014/Aufklaerung_Einwilligung_Biobanken_e.pdf

Further use of anonymised samples

142 Under the HRA, a differentiated regime is also established for the further use of anonymised samples and data for research. Research involving anonymised biological material and anonymously collected or anonymised health-related data is excluded from the scope of the HRA and thus not subject to any regulations (Art. 2 para. 2 lets b and c HRA). As regards the process whereby samples and data are anonymised for research purposes, the provisions of Art. 32 para. 3 HRA are to be noted, under which biological material and genetic data may be anonymised if the person concerned or the legal representative or next of kin have been informed in advance and have not dissented to anonymisation (**right to dissent**). In contrast, the anonymisation of non-genetic data for research purposes is not legally restricted.

143 It may be asked whether these regulations do not go too far: the provisions cover cases where samples and data obtained by physicians or hospitals/laboratories, with the consent of the person concerned, in a diagnostic or therapeutic context are then anonymised and used or transferred for research purposes. In such cases, no *personal* data ends up in the hands of third parties. There is, however, a certain risk that anonymisation may not be correctly performed, or that anonymised samples and data may subsequently be re-identified by third parties (cf. marg. no. 51). This being so, the right to dissent would appear to be justified at least in cases where there is an intention to **transfer** anonymised samples and data **to third parties for research purposes**. If, however, the samples and data remain within the institution where they were collected for diagnostic or therapeutic purposes, there would appear to be no interest worthy of protection in a right to dissent to the anonymisation of samples and data for research purposes. For in such cases, data protection risks are not increased, but are reduced as a result of anonymisation.

144 The situation is different in cases where samples and data are first transferred to a biobank in an identifying or pseudonymised form and are then **anonymised by the biobank**. In such cases, donors should be appropriately informed before consent is given or anonymisation is performed. This is because, as a result of anonymisation, donors can no longer exercise their right to revoke consent or their information rights (marg. no. 121).

Revocation of consent

145 Under Art. 7 para. 2 HRA, the persons concerned may revoke their consent at any time without giving a reason. This also applies to donors of biological material. If consent is revoked, the material and personal data of the person concerned is to be anonymised after data evaluation has been completed (Art. 10 HRO). As a more radical option, provision could be made for the **destruction** of the material and data.

146 To ensure that the right to revoke consent can be effectively exercised, the goals, topics, investigators responsible and main sources of funding should be made **transparent**, in a general manner, for the research projects conducted with the samples and data held by a biobank. Information should be provided via suitable channels, e.g. on the biobank's website, and can be made accessible exclusively to donors.

Exemption from informed consent

147 Exceptions to the requirements for informed consent and the right to dissent are specified in Art. 34 HRA. Under this **escape clause**, exceptions are permissible – with authorisation from the responsible ethics committee – in cases where (a) obtaining consent or providing information on the right to dissent is impossible or disproportionately difficult or would impose an undue burden on the person concerned, (b) no documented refusal is available, and (c) the interests of research outweigh other relevant interests. This clause is vaguely worded ("impossible", "disproportionately difficult", "undue burden") and needs to be defined in more concrete terms by the ethics committees, possibly with additional recommendations issued by the Federal Office of Public Health (on the basis of Art. 55 para. 4 HRA).

148 One possible application for the escape clause is the **transfer** of samples and data from one biobank to another (marg. no. 101). However, exemption from the consent requirements can only be contemplated if the receiving biobank guarantees the same level of data protection and data security and does not pursue purposes different from those of the biobank of origin. In general, these conditions can only be effectively assured for biobanks in this country.

149 If samples and data are transferred **abroad** in an identifying form or pseudonymised (together with the key), application of the escape clause should be ruled out even if equivalent protection of privacy is guaranteed by the legislation of the destination country. This is because donors or their relatives must be allowed to decide for themselves whether and to what extent they have confidence in the robustness and enforcement of foreign data protection standards. This is in line with the provisions of Art. 42 HRA, which state that biological material or genetic data may only be exported for research purposes if informed consent has been given by the person concerned (para. 1). In contrast, non-genetic health-related personal data may be disclosed abroad for research purposes even in the absence of informed consent (para. 2), provided that the requirements specified in Art. 6 FADP are met, in particular if an adequate level of data protection is ensured abroad. Once again, this distinction between genetic and non-genetic health-related data is based on genetic exceptionalism (cf. marg. no. 141); in view of the fact that non-genetic health-related data can be just as sensitive as genetic data, the provisions of Art. 42 HRA should be reconsidered.

150 Exemption from the consent requirements may also be possible – with authorisation from the ethics committee – in cases where existing collections established for diagnostic or therapeutic purposes are made accessible for research (marg. no. 103). Here, a prerequisite is that the **reorientation** should not pose any additional risks to privacy. It is to be assumed that additional risks to privacy will arise if samples and data are transferred to third parties for research projects; in such cases, the escape clause should not be applied. However, if samples and data are only used by researchers within the institution who are not able to identify the donors (researcher biobank), the use of existing collections for research purposes will not generally involve any additional risks to privacy. An exception to this would be if samples and data leave the diagnostic or therapeutic context altogether and are therefore no longer protected by medical confidentiality; in addition, under certain conditions, they could legally be used in criminal proceedings (cf. marg. no. 166). It should also be a requirement that the value of the collection for diagnostic or therapeutic purposes is not reduced when it is made accessible for research; this would be the case in particular if the materials were consumed for research to such an extent that the diagnostic or therapeutic purpose could no longer be fulfilled. If these conditions are met – no transfer of samples and data to third parties, no access to samples and data for criminal justice authorities, and no reduction in diagnostic or therapeutic value – application of the escape clause is justifiable.

151 In addition, the **right to revoke consent** must not be compromised by the transfer or reorientation of a collection. The right to revoke consent at any time can only be effectively exercised if donors know which biobank is storing their samples and data. This means that donors have to be informed in a general manner about the procedure in question, and that the receiving or reoriented biobank has to fulfil its duties of transparency. If all these conditions are met, the responsible ethics committee – in order to facilitate research – can and should grant authorisation for the collection in question to be transferred or reoriented without consent being obtained from the donors concerned.

Time of consent

152 Art. 17 HRA specifies that consent to further use for research is to be obtained from the person concerned at the time materials are sampled or data is collected for diagnostic or therapeutic purposes, **if further use is envisaged from the outset**. The same applies if samples and data are obtained during a specific research project, e.g. a clinical trial, and subsequently used for further, as yet unspecified research projects.

153 These arrangements can be justified by the **practical needs** of research (cf. marg. no. 106). It is, however, disproportionate that penalties should be prescribed for cases where the consent of the person concerned is not obtained at the time of sampling (cf. Art. 62 para. 1 let. b HRA) – for the samples are collected in any case (for a diagnostic or therapeutic purpose, or for a specific research project). Penalties would be more appropriately prescribed for cases where the decision to donate for research purposes is improperly

influenced by inducements or pressure, e.g. the prospect of certain advantages or disadvantages in connection with subsequent medical treatment.

Financial incentives

154 Article 21 of the Convention on Human Rights and Biomedicine (Council of Europe 1997), which has been ratified by Switzerland, states that the human body and its parts shall not, as such, give rise to financial gain. In national legislation, Art. 9 HRA specifies a **prohibition of commercialisation** for biological materials (but not for data), with infringements being treated as misdemeanours (Art. 62 para. 1 let. c HRA). This prohibition does not cover compensation for costs incurred in connection with donation – e.g. travel expenses or loss of earnings (Dispatch HRA). It is not clear whether and to what extent the prohibition would prevent benefit sharing. The question arises, for example, whether it would be deemed to be illegal commercialisation if donors obtained free access to a commercially available diagnostic or therapeutic method developed with the aid of donated materials. Similar provisions are included, for example, in transplantation law, with donors being entitled to reimbursement of the costs of lifelong follow-up (cf. Art. 12 let. c Transplantation Ordinance).

155 An argument in favour of the prohibition of commercialisation is the fact that payment of donors tends to lead to a decline in readiness to donate (marg. no. 107). Whether this also applies to benefit sharing is, however, doubtful (marg. no. 108). In addition, it would be a matter for biobanks and researchers themselves to assess – and possibly accept – the risk of a reduction in donations. To this extent, the prohibition is somewhat **paternalistic**. That aside, the risk that, as a result of payment, donors in financial difficulties could be exploited is far lower than in the case of organ donation for transplantation purposes. Nor is it a question, in the present research context, of protecting the health of transplant recipients. In addition, one can scarcely speak of a violation of human dignity – in the sense of complete instrumentalisation for the benefit of third parties – if appropriate compensation is provided for the removal of biological material.

156 From a **systematic legal perspective**, the prohibition of commercialisation is not consistent with the right – enshrined in Art. 14 para. 1 HRA – to be appropriately remunerated for participation in a research project with no expected direct benefit. The prohibition is all the more questionable as it does not cover the data transcribed from biomaterials (e.g. genetic and epigenetic information). Thus, a number of arguments would support the introduction of provisions along the lines of Art. 14 para. 1 HRA (appropriate remuneration), replacing the prohibition of commercialisation in research. Of course, in doing so, Switzerland could possibly be contravening the Biomedicine Convention and would be taking an exceptional course, since – as far as can be seen – the principle applicable in all EU countries is that the donation of human tissue, like blood donation, is not remunerated. As an alternative, the prohibition of commercialisation could be

given a restrictive interpretation and only applied to cases where compensation is paid directly for biomaterials, with exemptions for the sharing of benefits from commercialisable research results and for facilitated access to treatment methods. An interpretation of this kind would also be consistent with the sharing of benefits resulting from scientific research as provided for in Art. 15 of the Universal Declaration on Bioethics and Human Rights (cf. marg. no. 109).

Deceased persons

157 In deceased persons, the sampling of materials for biobanks is covered by the **extended consent system**, with general consent being permissible; in the case of deceased persons whose death occurred more than 70 years previously, research may be carried out without consent, unless such research is opposed by the **next of kin** (Art. 36 HRA). Special provisions are included in Art. 38 HRA: small quantities of body substances removed in the course of an autopsy or transplantation may be anonymised for research purposes without consent, in the absence of a documented refusal of the deceased person.

158 The question arises whether, in order to facilitate research, the dissent system specified in Art. 38 HRA should be generalised and also applied to the removal of materials from deceased persons for research purposes outside the context of an autopsy or transplantation. Here, the right to dissent would certainly also have to be granted to relatives. A possible argument supporting an **extended dissent system** of this kind is the fact that posthumous removal of samples for research purposes – unlike the removal of organs for transplantation – only affects privacy rights to a limited extent, if at all (marg. no. 117). However, the privacy rights both of the deceased person and of the relatives are only fully safeguarded with an (extended) consent system. Here – going beyond existing law – the consent system should be expanded to cover the sensitive (i.e. genetic and other health-related) data of deceased persons, if such data is to be used in a non-anonymised form.

Data protection and data security

159 It is clear from Art. 32 HRA that biological materials and genetic data which are stored for future, as yet unspecified research projects have to be **pseudonymised** (coded) or anonymised. Under current law, pseudonymisation must take place when storage begins – it is not sufficient for materials and data to be pseudonymised only when they are transferred to external research teams (cf. Art. 24 HRO). These regulations are inappropriate, particularly for collections which are held in a therapeutic context and additionally used for research purposes. To ensure data protection, it is crucial that samples and data cannot be identified by researchers themselves. The obligation to pseudonymise samples and data for storage from the outset should be replaced by more proportionate regulations requiring pseudonymisation to be carried out as rapidly as possible and at the latest before samples and data are transferred to researchers

(as specified in SAMW 2010b, no. 7.3 – but not in SAMW 2010a, no. 5.3). The same applies if the biobank envisages complete anonymisation of samples and data.

160 In addition, under Art. 43 HRA, anyone who **stores** biological material or health-related personal data for research purposes must take appropriate technical and organisational measures to prevent unauthorised use thereof, and fulfil the operational and professional requirements. In the HRO, the duties of care concerning the storage of samples and data are defined in detail (Art. 5), and requirements are specified for correct and secure anonymisation and coding (pseudonymisation) (Arts 25–27). To assure compliance with data protection and data security standards, biobanks should be required to obtain appropriate **certification** from an accredited certification organisation (cf. Art. 11 FADP).

161 If a biobank's data is stored in a **cloud system abroad**, donors – in view of the associated risks to privacy (marg. no. 125) – should be explicitly informed of this in advance. If a biobank only decides subsequently to store data in a non-Swiss cloud, it should also be required to obtain consent from the donors concerned; in such cases, merely informing the donor population so as to enable dissent does not appear sufficiently effective to safeguard the right to informational self-determination. The requirement to obtain **individual consent** to the storage of data abroad goes beyond the current regulations, which do not call for any precautionary measures if data is transferred abroad in an anonymised or pseudonymised form (without keys) (cf. Art. 42 HRA and Rütsche & Anner 2015, marg. no. 7).

162 The required technical and organisational measures essentially reflect internationally recognised standards. However, one point appears disproportionate – the requirement (specified in Art. 5 para. 1 let. c and Art. 5 para. 2 let. a HRO) that, when health-related personal data and biological materials are handled, all processing operations essential to ensure **traceability** are to be documented. Traceability is of crucial importance when biological materials are transplanted to third parties or used in the manufacture of therapeutic products. In such cases, traceability serves to protect patients' health. In a pure research setting, however, the protection goal is not relevant. Traceability thus serves merely to provide evidence in the event of data being manipulated or otherwise misused. At least in relation to biological materials, therefore, the traceability requirement should be abandoned. This would not affect donors' right to be informed about clinically relevant findings (marg. nos 127 ff.) as long as the samples can still (via a code) be linked to the donors.

163 The current legislation does not include any provisions concerning the organisation of biobanks. Here, appropriate regulations should be adopted to ensure that biobanks are **independent** – in terms of **organisation, personnel and financing** – of institutions that could misuse stored data to the detriment of donors.

164 Personal data stored in biobanks is not adequately protected by **criminal law**: Art. 321bis para. 1 of the Swiss Criminal Code ("Breach of professional confidentiality in research involving human beings") presupposes that a professional secret is disclosed without authorisation. Likewise, the contravention (applicable on a subsidiary basis) defined in Art. 35 FADP requires sensitive personal data or personality profiles to be disclosed without authorisation. If, however, samples cannot – even with a certain amount of effort – be traced back to the donor, then the transfer of such data does not constitute either the disclosure of a professional secret or the disclosure of personal data. If, for example, biobank staff or researchers themselves transfer pseudonymised samples and data (without the relevant key) to an insurer, then this presumably, under current law, does not represent a breach of professional confidentiality as defined in criminal and data protection law. Given the risk of re-identification of data, this appears problematic. Accordingly, consideration should be given to provisions which impose penalties on the unauthorised transfer of pseudonymised samples and data – i.e. transfers not covered by the donor's consent, the law, or ethics committee authorisation. Penalties should also be imposed for unauthorised re-identification and incorrect anonymisation of samples and data.

165 Also worthy of consideration is a criminal-law **prohibition on exploitation**. This would mean that public or private institutions or individuals (e.g. police authorities, health insurers or employers) who unlawfully obtain personal data from biobanks must not use it to the detriment of the donors concerned.

166 Attention is also drawn to the fact that the competent **criminal justice authority** can force materials or data used for research purposes to be handed over for use as evidence in criminal proceedings if the interest in establishing the truth outweighs the interest in preserving confidentiality (cf. Art. 265 para. 2 let. b in conjunction with Art. 173 para. 1 let. a CrimPC). Public trust in the biobank as an institution and in research could be strengthened if legislation precluded criminal justice authorities from accessing samples and data stored in biobanks. In some countries, regulations exist which prohibit access to research biobanks for police and criminal justice authorities, e.g. in Estonia (Art. 16 of the Human Genes Research Act). As long as criminal justice authorities are entitled, under certain conditions, to access samples and data made available for research, donors should always be informed of this fact in advance.

Communication of research results

167 Under Art. 8 HRA, donors have a right to be informed about results relating to their health. The information is to be communicated in an appropriate manner. Donors may choose to forgo such information (**right not to know**). No provision is made in the law for donors to be informed about the scientific results of research projects.

168 The scope of the right to be informed in accordance with Art. 8 HRA is not precisely defined by the Act. As mentioned above, it is not the task of researchers to make and communicate individual diagnoses. In addition, for biobanks and research projects with materials and data from large numbers of people, a duty to actively provide information can give rise to substantial costs (marg. no. 129). For this reason, the right to be informed is to be **narrowly interpreted**. According to the legislative materials, "clear evidence of a disease" is required, and the evidence in question must be "as far as possible conclusive" (Dispatch HRA, p. 8099). While this is to be accepted, information concerning genetic *susceptibilities* to disease should also be covered by the right to be informed, if the likelihood of the disease developing is considerable and effective preventive measures exist. This means, for example, that female donors should have a right to be informed if, in the course of a genome analysis, a mutation of the BRCA1 gene is incidentally discovered.

169 The communication of medically relevant findings by biobanks or researchers can involve substantial efforts and costs. Biobanks and researchers must therefore be free – with donors' consent – to adopt a **general policy of not reporting** individualised results. The right to be informed in accordance with Art. 8 HRA cannot be absolute; rather, it must be possible for it to be restricted, with the consent of the persons concerned (marg. no. 131). Prospective donors are, however, to be explicitly informed that any medically relevant findings which may be discovered cannot be reported.

5. Relationship between biobanks and researchers

170 With regard to the relationship between biobanks and researchers, two different situations are to be distinguished (marg. nos 32 f.): firstly, there are biobanks which transfer samples and data, or make them accessible, to third parties. In such cases – typical of large-scale biobanks – **material transfer agreements** are regularly concluded between the biobank and researchers. Secondly, researchers may be part of the same organisation as the biobank (so-called researcher biobank; marg. no. 33); here, researchers' access to samples and data is either unrestricted or governed by internal regulations.

171 From a normative perspective, questions concerning the relationship between biobanks and researchers arise **in three areas** in particular: under what conditions can researchers access a biobank (Sect. 5.1), what duties can and should a biobank stipulate for researchers (Sect. 5.2), and to what extent should biobanks (be allowed to) generate revenues and profits, or share in profits arising from research (Sect. 5.3)?

5.1 Access for researchers

Forms of access

172 In practice, researchers' access to biobanks takes **different forms** (Haga & Beskow 2008). Access may be restricted to members of the institution concerned (e.g. a hospital) or to participants in a research collaboration. But many biobanks are essentially open to all researchers – a simple request to make use of materials for scientific purposes may be sufficient. Biobanks which are pure databases often merely require user registration, and users may have to agree to the data protection provisions. Certain databases even allow completely unrestricted access. However, biobanks – especially the large national institutions – specify various conditions for the use of samples and data, with compliance being checked in each case[12]. In some countries, individual research projects also have to be reviewed by a (public) ethics committee.

173 Differences can also be observed with regard to the **form of transfer**: biological materials are physically transferred from biobanks so that researchers can work with them. As a result of repeated transfers, materials are gradually depleted, though researchers may be required to return remnants to the biobank. Data is generally stored electronically. Biobanks may allow researchers to access and process data on their own (or rented) servers, or to download data. Only in the latter case does a data transfer occur.

Conditions of use

174 In general, with regard to their distribution policy, biobanks should as far as possible be able to act **autonomously**. The entrepreneurial initiative which led to the development of a biobank should be reflected in the freedom to decide what type of research to support and to define the conditions of use. However, two qualifications need to be made.

175 Firstly, a biobank is bound by the wishes and legitimate expectations of donors – i.e. research projects are to be selected in accordance with the biobank's declared **purpose** (e.g. projects in the area of biomedical research in general or confined to specific conditions such as cancer, cardiac and pulmonary disease, rheumatic disorders, etc.). In addition, from the donors' perspective, it is crucial that their samples and data should make a contribution to scientific advances. Research projects must therefore satisfy **scientific quality requirements** with regard to the topic, method, researchers' expertise and available resources. Biobanks owe it to their donors to assess the scientific quality of the research proposals received, or to require that they be reviewed by an appropriate external body (e.g. an ethics committee).

176 Secondly, in selecting research projects, biobanks should respect the principle of **non-discrimination**. Selecting projects according to extraneous criteria (e.g. favouring

12 Cf., for example, the UK Biobank's principles of access: http://www.ukbiobank.ac.uk/ principles-of-access/

specific persons, research institutes or scientific schools) could undermine trust in biobanks as research infrastructure and would not be in the objective interests of donors. This does not mean that biobanks must be open to all researchers. The restriction of access to members of the same organisation or to particular research collaborations is legitimate if the collection has been developed by this organisation or collaboration. However, apart from such investment-based restrictions, any research team should have access to a biobank in accordance with the general conditions of use. If limited materials are available, it is appropriate to prioritise on the basis of the quantity required and the potential scientific benefits of the project[13].

Transparency of distribution

177 If it is to be equitable, the distribution of samples and data must be transparent. This concerns, firstly, the **conditions of use**, which should be published in an appropriate and universally accessible form. In addition, information on the **specific research projects** supported should be accessible, for donors at least. In particular, to give donors a sufficiently detailed picture, information is required on the research goal and topics, the researchers responsible and the main sources of funding for the project. The ability to obtain information on the projects supported means that donors can revoke their consent, should they so wish, in full awareness of the biobank's distribution policy (marg. no. 100).

178 For internal purposes and in view of possible inspections by supervisory authorities, the transfer of samples and data is to be adequately **documented**; in particular, material transfer agreements are to be retained.

5.2 Duties stipulated for researchers

179 As donated samples and data are their lifeblood, biobanks have an obligation to safeguard the interests of donors vis-à-vis researchers. In their dealings with researchers, biobanks are, as it were, donors' representatives. Donors, for their part, through the altruistic act of donation, seek to serve the common good (science or public health). This means that biobanks are also obliged to serve the common good and should pass this obligation on to researchers. Biobanks can represent the interests of donors and the public vis-à-vis researchers by stipulating appropriate requirements (duties) in **material transfer agreements** and, if necessary, enforcing these.

Data protection duties

180 The samples and data transferred by biobanks to researchers are, from the latter's perspective, anonymised, as they do not have access to the key (marg. nos 119 f.). However, particularly in the case of genetic data, it may be technically possible – with a certain amount of effort – for samples and data to be **re-identified**, i.e. linked

13 As in the case of the UK Biobank: http://www.ukbiobank.ac.uk/principles-of-access/

to the person concerned (marg. no. 51). In order to minimise this risk, it should be stipulated in biobanks' material transfer agreements that researchers are not to transfer to third parties the samples and data received or attempt re-identification themselves. Appropriate sanctions should be defined for violations, such as fines, exclusion from the biobank or even publication of the name of the offending party.

181 Data protection clauses in material transfer agreements are of particular importance when samples and data are transferred to **research teams abroad**. In such cases, because of the territoriality principle, the criminal-law provisions (cf. marg. no. 164) are not applicable. Here, unless the foreign state institutes criminal proceedings, data protection can only be enforced on the basis of contractual agreements.

Publication and registration

182 In the Declaration of Helsinki, the publication of – positive or negative – results of biomedical research in human subjects is described as an ethical obligation (WMA 2013, no. 36). In Switzerland, the Federal Council is empowered by Art. 56 para. 3 let. b HRA to specify that the results of clinical trials are to be published in public registries, although it has not yet done so. At the European level, a duty to publish a summary of the results of clinical trials in the EU database is specified in Art. 37(4) of the EU Regulation on clinical trials on medicinal products for human use. As regards the publication of results of research projects involving biological materials and data, **no regulations** exist in Switzerland.

183 Individuals donate biological materials for research in order to make a contribution to public health and the welfare of future patients. The realisation of these general benefits depends on the scientific results of research projects with donated samples and data being accessible for the biobank itself and for other researchers and medical practice. It follows that the results of research should be **published** in accordance with scientific standards (cf. marg. no. 133). As long as there is no duty to publish research results under applicable national law, such a duty should be stipulated in material transfer agreements. In addition, biobanks should ensure that the research projects supported are recorded in public **registries**, if such registries exist (cf. marg. no. 134).

184 In addition, it is increasingly being demanded that **raw data** from research projects should also be made available to other researchers (cf. Junod 2014). An open data policy is being pursued, for example, by the European Medicines Agency (EMA)[14]. Raw data is the unprocessed data on which the results of research are based. It includes, for example, the genetic information obtained from biomaterials in a research project. Raw data facilitates the interpretation of results, makes it possible to analyse how they were arrived at and can be used for further research. Biobanks are free to place researchers

14 Cf. http://www.ema.europa.eu/ema/

under a contractual obligation to make raw data available to third parties on request for scientific purposes.

5.3 Commercialisation of biobanks

185 At present, it can be assumed that most biobanks **do not operate for profit**, but distribute samples and data either free of charge or at a rate which merely covers the costs of biomaterial storage and handling and database operation. The issues of profit-making biobank activities and commercialisation of sample collections have been vigorously debated (European Commission 1998). Opponents of commercialisation argue that biobanks should take the form of non-profit organisations since tissue samples are donated free of charge and for altruistic reasons. Proponents, in turn, argue that commercialisation creates incentives for investment and thus indirectly promotes the common good.

Payment for transfers

186 Biobanks benefit from resources which are supplied by third parties voluntarily and free of charge. They should therefore, in return, have an obligation to serve the common good (cf. marg. no. 179). At the same time, the establishment and operation of biobanks requires considerable investments. Insofar as these are private investments, they enjoy the constitutional protection of economic freedom (Art. 27 FC). Accordingly, biobanks are entitled to operate for profit. If, however, biobanks are substantially funded by public monies, for-profit operation cannot be justified. It would not be acceptable for research to be impeded and made more costly as a result of publicly funded institutions pursuing their own commercial interests. It should therefore be ensured that the fees charged by publicly funded biobanks for making samples and data available to researchers do not exceed what is required to **compensate for their expenses**. What counts as – or goes beyond – compensation for expenses may be debatable in particular cases and depend in part on value judgements. It is not clear, for example, to what extent the salaries of biobank staff should come under the heading of compensation for expenses. A more precise definition of compensation for expenses could be included in guidelines to be issued, for example, by the SAMS or Swissethics (Swiss Ethics Committees on research involving humans).

187 For donors, it may be relevant whether they are contributing their samples and data to a for-profit or a non-profit organisation. To safeguard their right to self-determination, it would therefore be appropriate for **donors to be informed in advance as to whether or not the biobank is a for-profit organisation**. Non-profit status could, for example, be determined in the authorisation procedure (cf. marg. nos 194 ff.) and verified by the supervisory authority.

188 However, irrespective of whether a biobank is publicly funded or not, it must be free to make provision, in its material transfer agreements with researchers, for a

share in the profits arising from the research projects supported. This refers to profits generated by patented inventions and other commercially exploitable research results obtained with the aid of samples and data from the biobank (e.g. patented cell cultures, DNA sequences, pharmacologically active substances, diagnostic methods, etc.). Such provisions do not make research more expensive; rather, what is involved is the sharing of benefits between biobank and researchers. This does not amount to a morally unacceptable commercialisation of human biological materials. The only legitimate (protective) purpose served by the prohibition of commercialisation in the context of research is protection of the voluntary decision to donate (cf. marg. nos 107, 155 f.). This is not applicable to the biobank. Thus, whether and to what extent a biobank seeks to secure a share in profits generated by patented products frombiobank-based research will depend on its business model. It is therefore not essential that biobanks should take the form of non-profit organisations or units. Rather, benefit-sharing models can provide an incentive for patient groups – e.g. for thosewith a rare disease – to jointly establish a collection of samples for research purposes.

Licensing practices

189 Patent holders are accorded exclusive rights to utilise the patented invention. These rights include the authority to conclude commercial patent licence agreements and to choose the licensees. By pursuing **exclusive licensing practices** – i.e. granting licences to just one or a small number of licensees – patent holders can keep product prices at a high level.

190 In their material transfer agreements, biobanks are free to prohibit exclusive licensing practices with regard to patented inventions stemming from the biobank's samples and data. Patent holders would thus be obliged to offer utilisation of the patented invention to all parties on the same terms. For publicly funded biobanks at least, such clauses are to be regarded as an **ethical obligation**, given that exclusive licensing restricts patients' access to patented products and leads to increased healthcare costs.

191 Also conceivable are contractual agreements between biobanks and researchers which directly control the **price of patented products**, ensuring that they are affordable for the public and economically sustainable for the healthcare system.

5.4 Need for regulation

192 The relationship between biobanks and researchers is much less tightly regulated by current legislation, and also by international soft law (non-binding guidelines and declarations), than the relationship between biobanks and donors. From a regulatory perspective, **two key questions** arise: should legislators introduce provisions concerning researchers' use of samples and data, i.e. on material transfer agreements between biobanks and researchers? And should retrospective research projects involving samples

and data from biobanks require authorisation, or would it not be more appropriate for biobanks as such to be subject to mandatory authorisation and supervision?

Provisions concerning material transfer agreements

193 Apart from general contract law, there appear to be **no specific legal provisions** concerning material transfer agreements – except for the prohibition of commercialisation, under which payments for biological materials themselves are not permissible (Art. 9 HRA; cf. marg. no. 154). In general, biobanks should as far as possible be granted organisational and contractual freedom, so that initiatives of this kind can develop in the interests of biomedical research, the research/industrial location and public health (cf. marg. no. 174). However, in order to safeguard precisely these interests – as well as donors' interests – certain regulations should be considered. In particular, the following provisions would appear to be appropriate:

– Research projects are to be selected by biobanks in accordance with their **purpose** and on the basis of **scientific quality requirements**. In the selection of projects, the principle of non-discrimination is to be respected (marg. nos 175 f.).

– In the interests of **transparency**, biobanks' conditions of use are to be published. The transfer of samples and data is to be documented (marg. nos 177 f.).

– In order to **guarantee data protection**, biobanks must ensure that researchers do not transfer the samples and data received to third parties or attempt re-identification (marg. nos 180 f.).

– Biobanks must also ensure that, as soon after the completion of the research project as possible, researchers **publish** the results in the form of a full report. In addition, they should ensure that the research projects supported are recorded, if possible, in public **registries**, and that **raw data** from research projects is made available to third parties on request for scientific purposes (marg. nos 183 f.).

– The fees charged by publicly funded biobanks for making samples and data available to researchers should not exceed what is required to **compensate for their expenses** (as non-profit organisations). This does not preclude agreements to share in the profits arising from patented inventions or other commercially exploitable research results (marg. nos 186 ff.).

– Publicly funded biobanks should ensure that researchers **do not conclude exclusive licence agreements** concerning patented inventions (marg. nos 189 f.).

Authorisation and supervision

194 As long as personal identifiers are removed, the transfer of materials and data from a biobank to researchers does not require renewed consent from donors or the provision of further information (cf. Arts 32 and 33 HRA). However, research projects involving materials and data from biobanks do require **authorisation** from the responsible ethics committee (Art. 45 para. 1 let. a HRA, Arts 33 ff. HRO), unless the materials or data are irreversibly anonymised (Art. 2 para. 2 HRA). This is generally not the case for samples and data stored in biobanks; instead, they are typically pseudonymised (coded).

195 The legal requirement for mandatory authorisation of each individual research project is disproportionate, for the following reasons.

- The **need to protect** donors is absent or at least negligible, since, from the researchers' perspective, the samples and data are anonymised. To prevent attempts at re-identification by researchers, more effective means are available – namely, criminal-law provisions (yet to be drafted) and prohibitions (including sanctions) in material transfer agreements. In addition, criminal law is already applicable in cases where researchers disclose re-identified data (breach of professional confidentiality in research involving human beings under Art. 321bis SCC).

- The **appropriate and scientific use** of donated samples and data can and should be evaluated by biobanks themselves. In addition, as long as there is transparency regarding biobanks' distribution practice, donors can ascertain themselves whether their samples and data are being appropriately used, and, should they so wish, revoke their consent.

- Lastly, mandatory authorisation only applies to research projects in this country; projects conducted **abroad** – but with samples and data from donors in Switzerland – are not liable to such authorisation.

196 Mandatory authorisation for retrospective research projects involving materials and data from biobanks is thus neither appropriate nor necessary to protect the interests of donors or more general interests. On the contrary, it imposes an unnecessary burden on research. The resultant infringement of freedom of research is **not justifiable**.

197 If anything, mandatory authorisation should apply to those activities which involve risks to **donors' rights** and affect **public interests**. As discussed above (marg. nos 48 ff.), risks to donors arise firstly from the sampling of biomaterials (risks to personal integrity) and the collection of data (risks to privacy), and secondly from the storage of samples and data in a biobank and the transfer of materials to third parties (risks to privacy). In addition, the distribution of samples and data to researchers is of general relevance given the importance of research, the research location, public health and healthcare costs.

198 Under current law, mandatory authorisation already applies to the **sampling** of biological materials and the collection of health-related data for research purposes (cf. Arts 14 ff. HRO). However, the **further use** (storage and transfer), for research purposes, of samples and data already collected is not in itself subject to mandatory authorisation. This contrasts with the situation in various other countries, where biobanks are approved or accredited and supervised by national authorities (European Commission 2012).

199 Authorisation would need to take the form of an **operating licence for biobanks**, covering donor recruitment, storage and transfers of samples and data. As regards recruitment, the risks and burdens of sampling and data collection would have to be assessed and weighed against the potential benefits for research supported by the biobank. With regard to the storage of samples and data, the organisation of the biobank, in particular, would have to be evaluated, as well as measures to prevent unauthorised access to samples and data. Further prerequisites would be that the conditions of use are transparent, and that samples and data are distributed in such a way as to ensure that the biobank is actually useful for research. In addition, the compliance of material transfer agreements with legal requirements (yet to be specified) would have to be monitored by supervisory authorities.

200 Operating licences, and the conditions to be met, would need to be legally regulated. The operating licence would then supersede the authorisations required for each individual research project under current legislation. Biobanks should be **given the choice** of either obtaining an operating licence or declining to do so, with researchers then still being required to obtain a specific authorisation for each project. The optional nature of the operating licence would also mean that no problems relating to transitional legal arrangements would arise. Rather, each biobank would be free to decide whether and when to switch from the project authorisation to the operating licence regime.

201 As regards the granting of operating licences for biobanks, there are good reasons to assign responsibility to the **cantonal ethics committees**. Firstly, authorisation for individual research projects is already granted by these committees. Secondly, under current law, the ethics committees are responsible for approving exemptions from informed consent to further use of samples and data (in accordance with Art. 34 HRA). In particular, such exemptions could include, under certain conditions, the transfer of samples and data to other biobanks (marg. nos 148 f.).

6. Conclusions

202 This Opinion summarises the **key facts** concerning biobanks for research and addresses the **central ethical and legal issues** involved. Following an introduction to the topic (Chap. 1), various types of biobanks were distinguished and the associated terminology

was discussed (Chap. 2). This was followed by an exploration of the potential benefits and risks of biobanks from a medical and ethical perspective; the discussion considered both specific and more general questions, illustrating the numerous ways in which the opportunities and risks arising from biobanks are related to the ethical principles of autonomy, non-maleficence, beneficence, justice, solidarity, participation and trust (Chap. 3). The next two chapters dealt with a variety of concrete issues involved in the relationship between donors and biobanks (Chap. 4), and between biobanks and researchers (Chap. 5). In each case, in the light of the current legal framework, it was asked whether there is a need for regulation and, if so, what kind of provisions should be adopted. These regulatory proposals are also included in the Commission's recommendations below (Chap. 7).

203 In retrospect, it is apparent that specific problems and conflicting interests cannot be resolved directly on the basis of the relevant **ethical principles**. However, a principle-based approach provides valuable guidance in recognising the general significance of specific problems, placing them in a broader normative context and comparing them with similar issues arising in other areas of medicine and society. In addition, the principles make it possible to identify the goods and interests at stake in a specific conflict situation, and show how the opposing positions are to be weighed up. To this extent, in terms of methodology, the principles discussed in Chap. 3 and the reflections on specific problems in Chaps 4 and 5 are closely interrelated.

204 In general, the discussion of the **need for regulation** indicates that current research regulations in Switzerland are not essentially geared to the particular institutional features of biobanks. As regards the density of regulation, there are considerable differences between the relationship between donors and biobanks on the one hand, and between biobanks and researchers on the other.

– The **relationship between donors and biobanks** is governed by the detailed and varied provisions of human research law on the handling of biological materials and health-related personal data for research. In certain respects, these provisions appear to be overly restrictive and not necessary for the protection of individuals who make their samples and data available to a biobank for research. To this extent, freedom of research is excessively restricted, and the Human Research Act's declared aim of creating favourable conditions for research (Art. 1 para. 2 let. a HRA) cannot be achieved in the area of biobank-based research. Conversely, current law lacks important privacy and data protection safeguards, e.g. a duty to inform donors about the essential institutional aspects of biobanks, transparency requirements concerning the activities of biobanks, criminal-law protection of pseudonymised data, a prohibition on the use of illegally obtained samples and data to the detriment of donors, or safeguards preventing criminal justice authorities from accessing donors' data.

– In contrast to the protection of donors' privacy and data, the **relationship between biobanks and researchers** is scarcely regulated. There is a general lack of provisions recognising the participatory interests of donors and the obligation of biobanks to serve the common good, e.g. in the form of donors' rights to share in profits, researchers' rights to access biobanks, or a duty to publish research results obtained with the aid of biobanks.

7. Recommendations

205 On the basis of the foregoing ethical and legal considerations, the Commission offers the following recommendations:

1. The autonomy of donors should be strengthened:

– Prior to the collection or further use of their samples and data by a biobank, donors should be adequately **informed about the biobank as an institution** (purpose and organisation of the biobank, arrangements for the storage of samples and data, procedures for the selection of research projects, and the biobank's for-profit/non-profit status) (marg. nos 94 ff., 140, 187).

– General consent should always be obtained for the **further use of samples and data** in pseudonymised form; it is not sufficient merely to grant a right to dissent in relation to non-genetic health-related data (rejection of genetic exceptionalism) (marg. no. 141).

– To ensure that donors can effectively exercise their **right to revoke consent**, biobanks should provide general information, via suitable channels, on the research projects supported (in particular, on the research goal and topics, the researchers responsible, and the main sources of funding) (marg. nos 146, 177).

– If consent to further use of samples and data for research purposes is obtained **prior to medical treatment**, it should be ensured that the decision to donate is not improperly influenced by inducements or pressure in this regard; criminal-law penalties should be prescribed for the exercise of improper influence (marg. no. 153).

– Donors should be informed that, under current legislation, samples and data made available for research can, under certain conditions, be **used as evidence in criminal proceedings** (marg. no. 166).

2. **More effective measures should be taken to protect data stored in or transferred by biobanks**:

   – To assure compliance with data protection standards, biobanks should be required to obtain appropriate **certification** from an accredited certification organisation (marg. no. 160).

   – If a biobank's data is stored in a **cloud system abroad**, donors – in view of the associated risks to privacy – should be explicitly informed of this in advance. If a biobank only decides subsequently to store data in a non-Swiss cloud, consent should also be obtained from the donors concerned (marg. no. 161).

   – Appropriate regulations should be adopted to ensure that biobanks are **independent** – in terms of organisation, personnel and financing – of institutions that could misuse stored data to the detriment of donors (marg. no. 163).

   – Samples and data stored in biobanks should be more effectively protected by **criminal law** (penalties should be imposed for the unauthorised transfer of pseudonymised samples and data to third parties, unauthorised re-identification and incorrect anonymisation; a criminal-law **prohibition on exploitation** should be introduced) (marg. nos 164 f.).

   – Legislation should preclude **criminal justice authorities** from accessing samples and data stored in biobanks for research purposes (marg. no. 166).

   – Biobanks should ensure that researchers do not **transfer** to third parties the samples and data received or attempt r**e-identification** thereof (marg. nos 180).

3. **The legal framework for biobank-based research should be improved**:

   – For the **sampling of biological materials** and the collection of data for a biobank, it is sufficient that donors should be informed about the biobank as an institution. Given the minor nature of the intervention, it is not necessary that donors should be informed about the specific research project (marg. no. 137).

   – If a collection established for diagnostic or therapeutic purposes is to be **anonymised** for research purposes, donors do not need to be informed in cases where the anonymised samples and data will not be transferred to third parties (marg. nos 143 f.).

   – If samples and data are **transferred** from one biobank to another (in an identifying form or pseudonymised, together with the key), exemption from informed consent

requirements should be permissible with authorisation from the responsible ethics committee. The receiving biobank must, however, guarantee the same level of data protection and data security and not pursue purposes different from those of the biobank of origin; it must therefore be located in this country. In addition, donors should be informed about the transfer in a general manner (marg. nos 148 f., 151).

– If a collection established for diagnostic or therapeutic purposes is made accessible for research (**reorientation**), exemption from consent requirements should also be possible, with authorisation from the ethics committee, provided that the samples and data are not transferred to third parties, they cannot be accessed by criminal justice authorities, and the diagnostic or therapeutic value of the existing collection is not reduced; in addition, donors should be informed about the reorientation in a general manner (marg. nos 150 f.).

– Biobanks should be required to **pseudonymise** (or anonymise) stored samples and data as rapidly as possible and at the latest before they are transferred to researchers; it is not, however, necessary that they should be pseudonymised from the outset (marg. no. 159).

– The **prohibition on commercialisation** should be restricted to cases where compensation is paid directly for biomaterials, with exemptions for the sharing of benefits from commercialisable research results and for facilitated access to treatment methods (marg. nos 155 f.).

– With regard to samples stored in biobanks, it is not necessary to document all processing operations that are required to ensure **traceability** (marg. no. 162).

– Biobanks and researchers must be free – with donors' consent – to adopt a general policy of **not reporting medically relevant findings**; prospective donors should be appropriately informed of any such policy (marg. no. 169).

– Provision should be made for an **optional operating licence** for biobanks, which would supersede the authorisations required for each individual research project under current legislation; responsibility for granting operating licences could be assigned to the cantonal ethics committees (marg. nos 194 ff.).

4. Biobanks should increasingly be obliged to serve the common good:

– Research projects should be selected in accordance with the biobank's declared **purpose** and on the basis of **scientific quality requirements**; in the selection of research projects, the principle of non-discrimination is to be respected (marg. nos 175 f.).

– Biobanks must publish their **conditions of use**. Transfers of samples and data are to be documented (marg. nos 177 f.).

– Biobanks must ensure that the results of research are **published** as soon after the completion of the research project as possible. In addition, biobanks should ensure that the research projects supported are recorded in public **registries**, if this is possible, and that **raw data** from research projects is made available to third parties on request for scientific purposes (marg. nos 183 f.).

– The fees charged by publicly funded biobanks for making samples and data available to researchers should not exceed what is required to **compensate for their expenses** (as non-profit organisations); this does not preclude agreements to share in the profits arising from commercially exploitable research results (marg. nos 186 f.).

– Publicly funded biobanks should ensure that researchers do not conclude **exclusive licence agreements** for patented inventions (marg. nos 189 f.).

5. The recommendations are to be implemented in the form of amendments to legislation and ethical guidelines; public debate on biobanks should be promoted by appropriate means:

– Implementation of the recommendations concerning biobanks for research calls for various amendments to the current Human Research Act and the associated Human Research Ordinance. In addition, new legal provisions are required, e.g. new criminal offences to protect samples and data stored for research. From a technical legal viewpoint, all these changes could probably best be put into effect via a **specific Biobanks for Research Act**.

– Where no new regulations or changes to existing legal provisions are necessary, the recommendations can be implemented in the form of **ethical guidelines**. Such guidelines could cover, for example, the following questions: What specific elements should be included in the information provided with a view to obtaining general consent? What requirements should be specified for a biobank's independence? What costs incurred by a biobank come under the heading of (legitimate) compensation for expenses? What points should be dealt with in material transfer agreements between biobanks and researchers? This is primarily a task for the SAMS, which has already issued guidelines (withdrawn at the beginning of 2014) and recommendations on biobanks.

– Regardless of whether a legislative approach is pursued or guidelines are developed, the Commission takes the view that **public attention** should increasingly be focused on biobanks and their implications for society and the healthcare system. Even if

public debate tends to emerge primarily from civil society, institutions and authorities in the health sector are also free to promote public engagement with the topic of biobanks.

Annex

Box 1: Lausanne Institutional Biobank (BIL)

The Lausanne Institutional Biobank (BIL), set up in 2013 by the Lausanne University Hospital (CHUV) and the University of Lausanne (UNIL), is the only hospital-based research biobank project of its kind in Europe (unique in terms of its systematic approach, the genome sequencing provided and the possibility of re-contacting patients). The biobank was established using samples donated by CHUV hospital patients. The primary goal of the BIL is to collect a large number of blood samples – linked to patient data – from which DNA can be extracted. The samples are frozen and retained for an indefinite period. They are linked to information on patients' education, occupation and ethnicity, as well as all the clinical data in the CHUV medical records, and are made available for future, as yet unspecified (genetic and non-genetic) research projects. The samples and data are collected for diagnostic or therapeutic purposes and, after one-time general consent has been given by the donor concerned, they are deposited in the BIL. To date, 17,500 patients (75%) have consented to further use of their samples and genetic data for research purposes in coded form; 14% have withheld general consent, and 10% have only consented to further use of their samples and genetic data in anonymised form. The initial research projects approved and now underway relate to conditions such as Alzheimer's disease, liver disorders, stress cardiomyopathy and Parkinson's disease. A mother-child biobank (MOB) has also been established to promote research in pregnant women and newborns – populations often neglected in clinical research. Samples and data from the BIL can be made available to researchers who submit an appropriate application in connection with a research project. Applications are sent by e-mail, with the research protocol, to the BIL office, reviewed by BIL management and then forwarded to the cantonal ethics committee responsible for human research. If the project is approved, a material transfer agreement is signed, and the samples are released.

(Source: http://chuv.ch/biobanque, accessed on 10 December 2015)

Box 2: Pathology institute tissue banks

In the archives of their pathology institutes, university and central hospitals maintain their own tissue banks, with samples and data stored for an indefinite period and made available for biomedical research projects on request. Some of the samples, fixed in formalin, have been preserved for several decades. Certain tissue banks, such as that of the Zurich University Hospital Institute of Surgical Pathology, also contain "fresh" (i.e. deep-frozen) tissue samples. The samples are linked to the relevant pathology findings and possibly other patient data. In some cases, patient data is stored in coded form in an internal database; in other cases, however – e.g. in the Tissue Bank Bern (TBB) – it is only coded before being released

for use in a research project. Each transfer to a research team is subject to a material transfer agreement and is clearly documented.

(Sources: www.pathology.unibe.ch/forschung/core_facilities/tissue_bank_bern_tbb/index_ger.html; www.en.klinische-pathologie.usz.ch/expert-knowledge/pages/centralized-tissue-biobank-usz.aspx, accessed on 10 December 2015)

Box 3: Swiss Biobanking Platform

The Swiss Biobanking Platform (SBP), launched in 2015, is the national coordination platform for biobanks collecting human or non-human biospecimens. It was established under a joint initiative of the Swiss National Science Foundation (SNSF) and the Swiss Academy of Medical Sciences (SAMS). The main participants are currently the Institutes of Pathology at the University Hospitals of Basel, Bern and Lausanne.

The goal of the SBP is to meet the growing demands of research involving biological materials with regard to quality control, access to information, transparency and networking of biobanking activities. The SBP plans to produce a national online catalogue of biobanks, to promote the harmonisation of biobanking processes in accordance with international standards, and to provide information on legal and ethical issues associated with biobanking activities. The SBP also collaborates closely with the Biobanking and BioMolecular resources Research Infrastructure (BBMRI), serving as the Swiss contact point for this European organisation.

(Sources: http://p3.snf.ch/Project-154086; http://biobank-suisse.ch, http://oncosuisse.ch, http://swissbridge.ch, accessed on 10 December 2015; Mooser & Currat 2014; NEK-CNE hearing with Prof. Aurel Perren on 3 July 2015.)

Box 4: UK Biobank, UK Biobank Ethics and Governance Council and Framework

UK Biobank is a major national health resource, with the aim of improving the prevention, diagnosis and treatment of a wide range of serious and life-threatening illnesses – including cancer, heart diseases, stroke and diabetes. UK Biobank recruited 500,000 people aged 40–69 years in 2006–2010 from across the country to take part in this project. They have undergone measurements, donated blood, urine and saliva samples for future analysis, provided detailed information about themselves and agreed to have their health followed. UK Biobank is hosted by the University of Manchester and supported by the National Health Service (NHS).

The UK Biobank Ethics and Governance Council (EGC) is an advisory body with members appointed by the funders independently of UK Biobank. It has no formal regulatory role but rather advises UK Biobank in the manner of a "critical friend". The Ethics and Governance Framework (EGF) sets out the relationship between UK Biobank and participants, research communities, individual researchers and society. The EGF may be seen as an instrument, legitimised through wide discussion, which serves to align the public interests in research and the privacy and other interests of participants, as well as engendering trust. The EGC is charged with monitoring and reporting publicly on the conformity of UK Biobank with the EGF and advising more generally on the interests of research participants and the general public in relation to UK Biobank.

(Sources: www.ukbiobank.ac.uk/, accessed on 10 December 2015; Nuffield Council on Bioethics 2015, pp. 131 f.)

Box 5: International Cancer Genome Consortium

The International Cancer Genome Consortium (ICGC) has been organised to launch and coordinate a large number of research projects that have the common aim of elucidating comprehensively the genomic changes present in many forms of cancers that contribute to the burden of disease in people throughout the world. The primary goals of the ICGC are to generate comprehensive catalogues of genomic abnormalities (somatic mutations, abnormal expression of genes, epigenetic modifications) in tumours from 50 different cancer types and/or subtypes which are of clinical and societal importance across the globe, and to make the data available to the entire research community as rapidly as possible, and with minimal restrictions, to accelerate research into the causes and control of cancer. The ICGC facilitates communication among the members and provides a forum for coordination with the objective of maximising efficiency among the scientists working to understand, treat, and prevent these diseases. As of January 2015, 74 projects representing over 17 countries and jurisdictions had sequenced over 25,000 cancer tumour genomes. Samples are held by each member project, while data is deposited in a central repository located in Toronto, Ontario. The project distinguishes two "types" of data. Open access data, which does not contain obvious personal identifiers, is available from the ICGC Data Portal. Controlled access data, which is more readily identifying, is available to authorised researchers for approved research through the ICGC Data Compliance Office. After approval the researcher is able to download the data onto their own system for analysis.

(Sources: https://icgc.org/, accessed on 10 December 2015; Nuffield Council on Bioethics 2015, p. 140)

Box 6: The Psychiatric Genomics Consortium

The Psychiatric Genomics Consortium (PGC), which began in 2007, is the largest biological experiment in the history of psychiatry. It is an international initiative with over 500 investigators from over 80 institutions in 25 countries. There are more than 170,000 subjects currently under analysis. The purpose of the PGC is to conduct mega-analyses (individual-level data meta-studies) of genome-wide genetic data for psychiatric disorders. From 2007 to 2011, the PGC focused on autism, attention-deficit hyperactivity disorder, bipolar disorder, major depressive disorder and schizophrenia. It now includes large studies of anorexia nervosa, substance use disorders, obsessive-compulsive disorder/Tourette's syndrome and post-traumatic stress disorder. The PGC data repository is located in the Netherlands. All phenotype and genotype data is stored there, and all analyses of the data are carried out on the Genetic Cluster Computer.

(Sources: http://consortiapedia.fastercures.org/consortia/pgc/, accessed on 10 December 2015; Nuffield Council on Bioethics 2015, pp. 140 f.)

Box 7: Cloud storage

Cloud storage is a model of data storage where the digital data is stored in logical pools, the physical storage spans multiple servers (and often locations), and the physical environment is typically owned and managed by a hosting company. These cloud storage providers are responsible for keeping the data available and accessible, and the physical environment protected and running. People and organizations buy or lease storage capacity from the providers [e.g. Dropbox, Synaptop, AWSS3] to store user, organization, or application data.

(Source: http://en.wikipedia.org/wiki/Cloud_storage, accessed on 10 December 2015)

Box 8: PatientsLikeMe

PatientsLikeMe (PLM), the largest participant-driven research network, is a health data-sharing platform, founded in 2004 by three MIT engineers. PLM has more than a quarter of a million members representing over 2,000 health conditions. Through this company, people connect with others who may have the same disease or condition (e.g. cancer, amyotrophic lateral sclerosis, pulmonary fibrosis, diabetes, depression, macular degeneration), and track and share their own experiences. In doing so, they generate data about the real-world nature of disease that can help researchers, pharmaceutical companies, regulators and health providers develop more effective products, services and care. PLM allows members to contribute their own data about their conditions (treatment, history, side effects, hospital episodes, symptoms, function scores, weight, mood, quality of life, etc.) on a continuing basis. The resulting longitudinal record is organised into charts and graphs that allow members to

identify patterns, gain insight and place their experiences in context, as well as to see what treatments may have helped other patients like themselves. The website also gives members lists of relevant clinical trials, and they can search the site for trials for which they may be eligible. Today, PLM is a for-profit company, aligning patient and industry interests through data-sharing partnerships. The company also offers a commercial service to actively message potential participants for specific clinical trials.

(Sources: https://patientslikeme.com, accessed on 10 December 2015; Nuffield Council on Bioethics 2015, pp. 146 f.)

Box 9: openSNP

openSNP is a non-profit, open-source Web application project, which allows direct-to-consumer genetic test customers to publish their test results free of charge, together with phenotypic information, to find others with similar genetic variations and learn more about their results. openSNP was founded in 2011 by a team of young German biotechnology researchers.

(Source: https://opensnp.org/, accessed on 10 December 2015)

Box 10: Clinical Study Data Request

Clinical Study Data Request is a website which allows researchers to make further use of clinical trial data from pharmaceutical companies such as Astellas, Bayer, Boehringer Ingelheim, Eisai, GSK, Lilly, Novartis, Roche and Sanofi. Researchers can use the site to request access to anonymised patient-level data and/or supporting documents from clinical studies to conduct further research that can help advance medical science or improve patient care. Following approval, access is provided after the relevant study sponsor or sponsors have received a signed data sharing agreement. Under this agreement, the research team is required to, for example: only use the data for the agreed research purpose and not download or transfer the data for future use; protect the privacy and confidentiality of research participants (the researchers must not attempt to establish the individual identities of research participants); obtain any regulatory or ethics approvals necessary to conduct the analysis; inform the relevant sponsor(s) and regulatory authorities of any safety concerns as soon as they are identified; allow the relevant sponsor(s) to use any invention coming out of the research that impacts the ability of the sponsor to develop or commercialise their products (such use will be free of charge and throughout the world).

(Source: https://clinicalstudydatarequest.com, accessed on 10 December 2015)

Box 11: 23andMe

23andMe is a privately held genetic profiling company, founded in 2006 to provide genetic testing and interpretation to individual consumers. 23andMe began offering direct-to-consumer genetic testing in 2007 (with kits costing USD 99 in June 2015). Customers provide a saliva testing sample that is partially SNP genotyped, and results are posted online. The company offers customers an assessment of inherited traits and genetic disorder risks. In 2013, the US FDA ordered 23andMe to discontinue marketing its personal genome service (PGS) as the company had not obtained the legally required regulatory approval, resulting in concerns about the potential consequences of customers receiving inaccurate health results. However, 23andMe continues to offer its services in other countries, e.g. in the UK. The company may itself also carry out research using its customers' samples and information. The data generated may be reported, although it is not usually made available for wider research use. 23andMe may have the largest DNA database anywhere that is open for medical studies. According to the company, about 600,000 of its 820,000 customers have agreed to donate their DNA data for research purposes. The large pool of data in its customer database has also attracted the interest of academics and other partners, including pharmaceutical and biotechnology companies. It has been reported (e.g. by Forbes) that Genentech will pay as much as USD 60 million for access to 3,000 Parkinson's patients in 23andMe's database.

(Sources: https://23andme.com; http://en.wikipedia.org/wiki/23andMe; http://technologyreview.com/view/534006/23andmes-new-formula-patient-consent, accessed on 10 December 2015; Nuffield Council on Bioethics 2015, p. 10)

List of abbreviations and legislation

BBMRI	Biobanking and BioMolecular resources Research Infrastructure
CrimPC	Swiss Criminal Procedure Code of 5 October 2007 (Criminal Procedure Code, SR 312.0)
EMA	European Medicines Agency
FADP	Federal Act of 1 June 1992 on Data Protection (SR 235.1)
FC	Federal Constitution of the Swiss Confederation of 18 April 1999 (SR 101)
GWAS	Genome-wide association study
HGTA	Federal Act of 8 October 2004 on Human Genetic Testing (SR 810.12)
HRA	Federal Act of 30 September 2011 on Research involving Human Beings (Human Research Act, SR 810.30)
HRO	Ordinance of 20 September 2013 on Human Research with the Exception of Clinical Trials (Human Research Ordinance, SR 810.301)
ISBER	International Society for Biological and Environmental Repositories
MAGs	Medically actionable genes
Nagoya Protocol	Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity, concluded in Nagoya on 29 October 2010, entered into force for Switzerland on 12 October 2014 (SR 0.451.432)
NEK-CNE	Swiss National Advisory Commission on Biomedical Ethics
OECD	Organisation for Economic Co-operation and Development
PGS	Preventive genomic sequencing
SAMS	Swiss Academy of Medical Sciences

SCTO	Swiss Clinical Trial Organisation
TransA	Federal Act of 8 October 2004 on the Transplantation of Organs, Tissues and Cells (Transplantation Act, SR 810.21)
UNESCO	United Nations Educational, Scientific and Cultural Organization
VUS	Variants of unknown/uncertain significance
WGS/WES	Whole-genome/whole-exome sequencing
WHO	World Health Organization
WMA	World Medical Association

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