Legal Challenges and Strategies in the Regulation of Research Biobanking

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Abstract In this chapter, some of the legal challenges of research biobanking are discussed and illustrated by examples of possible analogies as well some comparative notes on the regulatory strategies adopted in the Nordic countries. Human biological material is compared with biological waste, raw materials, human beings, personal or nonidentifiable health data, and different kinds of public resources. It is concluded that the complex nature of human biobanks would seem to defy any attempt at a simplified regulatory analogy. Even so, it is clear that the application of more sophisticated analogical reasoning will still be valuable in the regulatory process and that policy makers must try to identify an appropriate combination of diverse approaches. While the international nature of biomedical research provides a strong incentive for more harmonised rules, the regulatory process is here further complicated by the plurality of religious, cultural, social and legal traditions, as well as issues of regulatory competence. Nevertheless, some degree of regional or even international consensus could certainly be reached with regard to less controversial areas and issues, and this potential must be further explored. The regulation of research biobanking should be perceived as an ongoing step-by-step process, rather than a problem that will soon be solved once and for all. In the short-term perspective especially, it must be expected that legal restrictions and administrative inconveniences may cause additional costs and delay or even prevent promising research. The long-term aim must be to serve the best interests of the public, by a careful balancing of the freedom of research against other fundamental rights and values.

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Introduction

For the past few decades, there has been a steadily increasing debate about the appropriate regulation and governance of research biobanking. Although the study of human biological material has always been an important part of medical research, new possibilities related to advances in the field of genetics have generated a growing demand for easily accessible biological samples and various types of associated data. The establishment of such research resources has been facilitated by the parallel development in information and communication technology, making it possible to store and process large quantities of data, with comparatively limited input of time, personnel, and money. It is widely believed that research on large-scale collections of human material and associated data will open up new prospects in improving the health of individuals and of humankind as a whole.[1]

At the same time, the creation and use of so called biobanks or genetic databases is still causing considerable regulatory problems. Researchers and biobank principals find it hard to establish what the relevant legal requirements pertaining to their activities really are. While expressing a wish for legal certainty, however, they are also anxious to avoid having their freedom of research and immaterial property rights threatened by unreasonable and impracticable demands and restrictions. Policy makers would, of course, be more than happy to provide appropriate and well-balanced regulations that offer adequate protection to all interests concerned, not least the freedom of research and the privacy rights of donors. Despite the fact that questions relating to further use of human tissue, as well as genetic testing and screening, have been on the agenda for decades,[2] many legislators are still finding it very difficult to determine what the rules should be.

One of the circumstances complicating the regulatory situation is that biomedical research is often based on extensive international collaboration and cross-border activities, whereas binding international rules are so far lacking in the specific area of biobank research. The fact that there is a vast variety of nonbinding declarations, recommendations, and ethical guidelines on biobanking, adopted by different organizations or advocated by groups of scientists, does not provide any immediate help to the researchers and biobank principals who are legally bound by the domestic laws of the countries in which they operate.[3] The variety of national regulatory strategies and material rules may thus obstruct cross-border biobank activities, but also make it more difficult for potential donors to foresee how their interests would be protected if samples were to be transferred to another country.

Even from the domestic perspective, however, the co-ordination and harmonisation of biobank regulation with legislation in related areas have proved to be highly problematic. In this chapter, some of the challenges involved in regulating human

[1] See for example OECD 2008 Draft Guidelines for Human Biobanks and Genetic Research Databases.

[2] For some early examples, see Milunsky and Annas (1976), Berg (1983), Knoppers and Laberge (1989), and WHO (1985) Community approaches to the control of hereditary diseases.

[3] Kaye (2006).

research biobanks will be discussed and illustrated by examples of possible legal analogies as well some comparative notes on the regulatory strategies adopted in the Nordic countries. The regulatory tools and issues of competency are also touched upon before the chapter is concluded by some words on the process of biobank regulation.

Human Research Biobanks: What Are They?

General Comments

As is often underlined, already the meaning of the term 'biobank' may in itself be debated. It seems to have come into use in the Nordic countries in the mid-1990s, starting with Denmark,[4] and is today widely used. Even so, there is no general consensus on the definition of a biobank, and a host of other terms are also used to label the same or similar concepts,[5] for example, tissue banks, collections of biological material, tissue collections, tissue repositories or bio-repositories, DNA banks, gene banks and genomic or genetic databases. Other alternative terms somewhat less common include bio-libraries and tissue libraries.

When the term biobank is used, it may not only refer to the actual biological materials, but also to the facilities where these are stored or to the institution responsible for the collection and storage of samples. An early Danish biobank definition was thus 'an institution where biological material and clinical information is collected and can be redistributed, either to serve the original donor or scientific, health administrative or health political purposes'.[6] Used as a verb, biobanking would normally refer to the organised collection and storage of human biological samples and associated data, in view of making them accessible for various biomedical or health-related purposes.

The German Nationaler Ethikrat defines biobanks as 'collections of samples of human bodily substances (e.g. cells, tissue, blood, or DNA as the physical medium of genetic information) that are or can be associated with personal data and information on their donors', and also underlines the twofold character of biobanks, as collections of *both* samples and data.[7]

Not all biobank definitions include the associated data, however. In the Icelandic legislation, a biobank is defined as 'a collection of biological samples which are permanently preserved', where biological sample means 'organic material from a human being, alive or deceased, which may provide biological information about him/her'.[8] The definition used in the Swedish Act on Biobanks in Health Care

[4] See for example Nielsen et al. (1996) and Hermerén (1997).

[5] Cf. Elger and Caplan (2006).

[6] Nielsen et al. (1996) and Riis (1997).

[7] Biobanks for research 2004: Opinion of the German National Ethics Council.

[8] Article 3 of the Act on Biobanks no. 110/2000.

comprises 'biological material from one or more human beings that is collected and preserved for an indefinite or limited period, and whose origin is traceable to an individual or individuals.'[9]

The definitions of population biobanks and genetic or genomic databases tend to have a stronger or even primary focus on the data aspects, for example in the HUGO Statement on Human Genomic Data bases, 2002: 'A genomic database is a collection of data arranged in a systematic way so as to be searchable. Genomic data can include inter alia, nucleic acid and protein sequence variants (including neutral polymorphisms, susceptibility alleles to various phenotypes, pathogenic mutations), and polymorphic haplotypes.' The OECD 2008 Draft Guidelines for Human Biobanks and Genetic Research Databases define human biobanks and genetic research databases as 'structured resources that can be used for the purpose of genetic research, which include: (a) human biological materials and/or information generated from the analysis of the same; and (b) extensive associated information.'

As a final example, the Council of Europe Recommendation Rec(2006)4 on research on biological materials of human origin includes also the long-term perspective in its definition of the particular concept of a population biobank:

'A population biobank is a collection of biological materials that has the following characteristics:

i the collection has a population basis;
ii it is established, or has been converted, to supply biological materials or data derived therefrom for multiple future research projects;
iii it contains biological materials and associated personal data, which may include or be linked to genealogical, medical and lifestyle data and which may be regularly updated;
iv it receives and supplies materials in an organised manner.'

It should be clear already from the examples provided that the language of biobanking is by no means a single universal language, but rather a group of languages or at least distinguishable dialects, where a word may have several different meanings and the same concept may be attributed different names. It may be self-evident that any regulatory project in this field would have to start by closely defining the proposed object of regulation, but also in international debate and co-operation it would be recommendable to beware of the risk for misunderstandings.

Human Material Removed and Stored for Various Purposes

This book is focussed on *research* biobanks, but human material and associated data may of course be collected and stored in biobanks for a number of other health-related purposes, such as patient safety and quality assurance in healthcare,

[9] Chap. 1, Sect. 2 of the Biobanks in Medical Care Act (2002: 297).

transplantation or transfusion, assisted procreation or the manufacturing of medicinal products. Many biobanks are in fact created and used for a mix of such purposes, which gives rise to the question whether or not the rules governing biobank research ever could or even should be universal. While a lot of the biobank debate of the 1990s would seem to have concerned issues related to the so-called *further use* of human tissue collected for diagnosis and treatment or leftover from surgical interventions, the samples stored in many of the large-scale biobanks or population-based genetic databases of the new millennium are normally intended for more long-term use in a variety of future projects that cannot be foreseen at the time when the samples and associated data are collected. Another category consists of biobanks originally established for use in a specific research project, but afterward preserved and used for other projects.

Different provisions could thus apply to human material removed, collected and stored for purposes related to for example:

- Diagnostics and treatment of individual donors/patients themselves
- Quality assurance and educational purposes in healthcare
- Assisted procreation or transplantation
- Health screening programmes
- Other health-related analysis, such as post-mortem examinations, protection against contagious diseases, insurance purposes
- Identification of individuals or familial relations in crime investigations, paternity cases, immigration matters, etc.
- The manufacturing of products

Research interests could concern the use of human materials originally collected and stored for:

- A particular research project or several specified projects
- Any of the purposes mentioned earlier, including *other* research projects
- Use in *future*, more or less unspecified, research projects

Depending on the original purpose for which the material was removed, collected or stored, different requirements for research-related use may be motivated. Whereas provisions on possible further use of different types of human materials would sometimes seem better placed in the legislation regulating the particular activity for which they were removed, it could also be argued that a comprehensive biobank legislation would have the advantage of providing overview and easier access to the relevant rules.

Type of Research Use Intended

From a regulatory perspective, the type of research for which the biobank materials are intended or used may also be highly relevant. As is clear from the above, many research biobanks are specifically focussed on the informational aspects of the biological material, in particular the genetic information. In this field, we could

find both clinical research projects and longitudinal epidemiological studies. Some projects may involve large-scale genetic screening with diagnostic or treatment implications for individual research subjects, thus blurring the borderline between epidemiological research and clinical research and between public health measures and individual health care.[10]

Other forms of research with human biological material may be primarily aimed at studying different functions or applications of the tissues, cells or genes as such, in a natural or manipulated form. This could involve the development of cell lines, new treatments or products or experiments in reproduction. When biobanks are established or used for this kind of purposes, they would not normally be referred to as genetic databases or DNA banks, but more often as tissue banks or cell banks. Here, the human material is used rather as raw material than as a source of information, which could of course motivate somewhat different rules. It is not unusual for banks with for example human ova, embryos or embryonic cells to be subject to special legislation.

Research use of human biological materials and associated data may also vary in relation to the duration of the storage. Some biobank regulations may be applicable only to banks specifically set up for long-term research purposes, whereas others have a much wider time frame, from very short storage to virtually endless.[11] This gives rise to the question if samples collected and used for their intended purpose more or less directly should also be considered to constitute biobank materials, even if they are never or only for a very short time stored in what could be viewed as a biobank facility? Other issues concern the point of time at which the sample begins to fall under the biobank regulation and the time when it ceases to be part of the biobank, having for example been transferred to another biobank, or having been destroyed, rendered non-identifiable or turned into a product. In some contexts, the term virtual biobank is used to describe 'a controlled (access) database on samples stored at different locations'.[12]

Policy Makers Are Still Struggling

When deciding on the type of activities and materials or data that should be covered by biobank regulation, legislators need to identify and carefully asses the different interests concerned, in order to determine the extent to which the arising legal issues

[10] One example can be provided by the heated debate concerning the Norwegian large-scale cohort study MIDIA, aimed at identifying environmental triggers of type 1 diabetes. This study, which included screening of 100,000 newborns and 15 years follow-up of the 2,000 children with high-risk genotype, had started in 2001 after having been approved by both the competent Research Ethics Committee and the Data Inspectorate. Nevertheless, in 2007 the project was stopped by the Directorate of Health, since it did not comply with the prerequisites for predictive genetic testing of children, prescribed in the Act on Biotechnology. See the decision of the Norwegian Directorate of Health 10.12.2007, 07/2904–19.

[11] Compare for example the Icelandic and Swedish Biobank Acts.

[12] See the Web page of the PopGen Database, http://www.popgen.info/Glossary.cfm.

are already adequately covered by existing regulation. In most countries, it is likely that at least some aspects of research biobanking will be covered by legislation regarding for example scientific research, patients' rights, use of human gametes or embryos, bio-patents or the processing of personal data. Even so, it is equally likely that certain aspects will be left out, and with regard to issues that *are* covered, it must be determined if the applicable rules provide satisfactory results in the particular context of research biobanking, by offering a balanced protection in view of *all* interests concerned, taking into consideration also long-term societal goals. In assessing their domestic regulation, legislators must furthermore consider not only the need for internal consistency and harmony between different areas of their own legal system, making sure that similar rules are applied in similar situations, but also compliance with public international law and other external requirements.

One strategy could then be to complement existing, general legislation with a minimum of provisions specifically related to biobanking and another to introduce more comprehensive specific biobank legislation. The point of departure could be the type of human material and data, or the intended use or potential misuse. New provisions could be primarily focussed on material rules, for example allowing or prohibiting certain activities or results, under stipulated conditions, or they could be aimed at securing appropriate procedures and oversight. Which strategy or combination of strategies to choose may not be self-evident.

Legal Analogies and Comparative Law

External and Internal Legal Comparisons

One of the methods widely used both in legal science and in the development of new legislation is comparative studies, whereby inspiration is sought from the solutions discussed or implemented in other jurisdictions. Such comparative legal research is also a necessary part of any attempt to reach consensus for international regulation. In new areas of for example rapidly developing technologies, however, the available material for this kind of legal comparison can be limited, making it all the more important to study existing regulation of *similar* activities, relationships and interests. The consideration of domestic legal analogies is in fact indispensable in any development of new regulation, if internal harmony, coherence and consistency of the legal system are to be achieved. Also in the interpretation and application of existing laws, analogy is an important tool, since no legal regulation can specify in detail all the cases and situations that should be covered.

Legal analogies of course presuppose that some area of similar activities and interests can actually be identified, which is one of the core problems in the regulation of biobanks. There is no lack of possible analogies that may seem plausible at first sight, quite the contrary, but at a closer look none of the alternatives quite measure up to the diversity and complexity that characterises the field of biobanking. Efforts to make adjustments by combining two or more analogies tend to bring

out conflicting principles. Nevertheless, a number of legal analogies have still been applied to biobank-related activities, comparing the human material to waste, raw material, human beings, personal or non-identifiable health data or a public resource. The analogies illustrate how human biological material has been perceived and regulated in different contexts and could thereby add to the understanding of the regulatory challenges and the strategies adopted in relation to biobanking.

Human Material as Biological Waste

A good place to start could be to look at the use of leftover or discarded human biological material, for example in the form of body parts or tissue removed in the course of a medical treatment, or blood samples having already been used for the intended diagnostic analysis. To the extent that the material is not needed for patient safety reasons, related to future care or treatment, the patient normally would not have any further use for the material and it could be regarded as biological waste, without value. In many countries, this kind of waste would be subject to certain rules regarding its disposal and destruction, for reasons related to the protection of environment, public health and safety. Even the patient himself or herself might not be allowed to bring his or her removed appendix home in a jar. An analogy based solely on the principles underlying such rules, however, would seem to imply that as long as discarded human biological material is handled in a competent way that does not constitute any danger to public health or environment; it should be free to use for research and perhaps also for other purposes. This policy has also been applied, at least to some extent. Although the waste analogy is not completely without relevance, however, it can quickly be discarded as insufficient since, indeed, in the words of George Annas, 'waste is not always what it seems'.[13]

Human Material as Raw Material

As opposed to being mere waste, certain types of human biological material have a long history of being attributed financial value, for example human hair. In the area of biomedicine, the human body is an important source of valuable raw material used to manufacture products or to be directly transplanted into other humans without previous processing. Not only materials such as blood or whole organs constitute precious resources, but even tissues that would otherwise have been regarded as biological waste could be sought after as raw material, for example placentas used for cosmetic products, medicines or stem cell research.[14] When human material is used as raw material or products, issues concerning patient and consumer safety become

[13] Annas (1999).

[14] See for example Annas (1988).

relevant, in addition to the previously mentioned more general requirements for the protection of environment and public health.

Another highly relevant legal aspect is that the use of human material in this context gives rise to questions related to the protection of property rights, in particular where products or inventions are developed from the material, as in the famous Moore case.[15] How should the human material be perceived at various stages of cultivation or manufacture?[16] Are for example cells and cell lines cultivated in vitro still just samples of human biological material, or do they constitute medicinal products? When does the biobank sample cease to exist, having been used up or turned into something else? Whether or not property rights could be part of an appropriate regulatory approach already to parts of the human body as such is a highly controversial issue.

Human Material as Part of the Human Being

Compared with other types of raw materiel, human biological material is undeniably different in the sense that it actually constitutes a part of a human being. This fact could motivate an analogy with the legal rules and principles applied in the protection of human beings, for example in relation to research, a field where an abundance of international and national regulations can be found.[17] Legal provisions in this field may be aimed at protecting the physical health and safety of the human being, which could of course be at risk at the removal of biological material, but may also focus on the bodily integrity and other privacy rights of the individual. Independent ethics review of research projects is often mandatory, and informed consent is a necessary precondition for virtually any research intervention.[18] Once the human biological material has been removed, however, the health-related risks would not be as prominent, but the protection of human dignity and privacy could still be of relevance to the prerequisites for lawful further use of any material removed.

Here, things start to get complicated. If human biological material as such does not merit quite the same protection as a living human being, which would perhaps seem a plausible conclusion, other familiar questions arise. What degree of legal protection should for example be offered to such human biological material as has a *potential* to develop into a full human being, i.e. embryos or human ova? And what

[15] Moore vs. Regents of the University of California, 793 P.2d 479 (Cal. 1990) Cal. Rep 146; see for example Laurie (2002) or for an early comment, Annas (1988).

[16] Cf. Rynning (2003a) at pp. 103–105.

[17] For extensive information on various rules and guidelines for research, see the Web resource CODEX of the Swedish Council for Research, http://www.codex.vr.se/codex_eng/codex/index.html.

[18] This is the first principle of the Nurnberg Code (1947), also laid down for example in the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects (first adopted in 1964), in Article 4 of the UN International Covenant on Civil and Political Rights and in Article 16 of the Council of Europe Convention on Human Rights and Biomedicine (1997).

about research interventions carried out when they can no longer constitute a threat to the donor's life or health, for example the taking of material from dead bodies or tissue from aborted foetuses? It soon becomes obvious that the legal protection offered to the body of a deceased human being and to certain types of biological material, such as human embryos,[19] ova or foetal tissue is quite different from the rules pertaining to biological waste or raw materials for products. The fact that not all types of human biological materials are attributed the same status, depending on their origin, potential function and the context in which they are removed from the body brings out the question of what determines the protection that should be offered to different categories of biobank material. Additional issues may arise when original properties of human material are radically changed, as for example is the case with so-called iPS cells,[20] or when mixed living human–animal material is created, as in so-called cybrid embryos. Apparently, also interests related to society as a whole, as well as donor relatives, must be considered. Nevertheless, the mere fact that a biological sample originates from a particular individual could have privacy implications related to this person's wishes to decide about its use. Does this mean that an explicit and specific informed consent is always needed or could it sometimes be sufficient merely to provide an opportunity to opt out?

Another principle considered to be based on respect for human dignity is that, as opposed to raw materials and products, human *beings* cannot be owned, bought or sold.[21] To what extent is it reasonable or even necessary that this principle of non-commercialisation be applied also to parts of the human body, in order to protect not only the human dignity of individuals, but also other societal values?[22] Certain activities, which could be envisaged as commercialisation or commodification of parts of the human body, are often thought to put such interests at risk.[23]

Human Material as Health-Related Personal Data

The issue of privacy rights naturally brings us to the analogy with rules pertaining to health-related personal data. This analogy would indeed seem appropriate, when research biobanking is primarily viewed as a way to make biological and medical data accessible for research.[24] The processing of personal data, and in particular

[19] Cf. Article 18 of the Council of Europe Convention on Human Rights and Biomedicine, demanding particular protection for embryos in research.

[20] Induced pluripotent stem cells, which are derived from adult body cells but have the ability to develop into any cell type, including germ line cells.

[21] Cf. Articles 4 of the UN Universal Declaration on Fundamental Human Rights (1948) and the European Convention for the Protection of Human Rights and Fundamental Freedoms (1950).

[22] See for example Nelkin and Andrews (1998).

[23] See Article 21 of the Convention on Human Rights and Biomedicine. Opposite view presented for example in Beyleveld and Brownsword (2001), pp. 192–194 and Laurie (2002), p. 299 ff.

[24] Already in some of its recommendations from the early 1990s, the Council of Europe voiced the idea that human tissue should be considered a source of information and be protected in the same

sensitive data such as health-related information, constitutes another highly regulated area, also at the international level.[25] Protection of privacy in this field is focussed on confidentiality and autonomy, although the protection offered is generally weaker and use of personal data without consent is more accepted than is the case with bodily interventions. The right to withdraw consent need not necessarily mean that data already collected must be erased. Other important interests, related to for example public health and freedom of research, thus carry great weight in this context.[26] Requirements on ethics review may also be less strict with regard to studies involving only data.

As part of their privacy rights, individual research subjects normally have a right of access to health information collected about them, but there may also be a right *not* to know. This brings out questions about feedback concerning research results and how to handle incidental findings that could be of relevance to the individual donor.

When genetic information is studied, there may be different opinions on who should actually be considered as 'the person or persons concerned' by the research.[27] Does the study of a particular person's genetic composition 'concern' only the individual from whom the biological material has been obtained, or does it concern also his or her close genetic relatives, the extended family or even a larger population? Who should then give consent and who should be informed? There are also other aspects of genetic information that have contributed to the debate on whether or not genetic data should be treated differently from other types of information, for example its ability to predict future development and risks.

Human Material as Non-Identifiable Health Data

Could there be situations where it would be reasonable to make an analogy with non-identifiable health data, i.e. data that cannot be traced to any identifiable individual? In relation to such data, protection of the freedom of expression and freedom of information will often be the overarching interests, implying that the data could

way as other media carrying personal information; see Recommendation R (92) 1 of the Committee of Ministers to member States on the use of analysis of deoxyribonucleic acid (DNA) within the framework of the criminal justice system and Recommendation R (92) 3 of the Committee of Ministers to member States on genetic testing and screening for health care purposes. See also Hondius (1997).

[25] See for example the Council of Europe Convention for the Protection of Individuals with regard to Automatic Processing of Personal Data (1981) and the Recommendation (97) 5 of the Committee of Ministers to Member States on the protection of medical data; Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data.

[26] In accordance with Article 8.2 of the European Convention of Human Rights, infringements of the right to private life may be justified provided they are in accordance with the law and necessary in a democratic society for the protection of certain other important interests, such as public health.

[27] See for example Gertz (2004) and Gevers (2005).

be freely accessed, used and disclosed. If we disregard the fact that for research purposes, de-identification of samples may not be acceptable for reasons of quality control, follow-up, etc., the question remains whether it would be at all possible to de-identify human material containing DNA. The answer would seem to depend on the definition of identifiability applied. In the explanatory memorandum to the Council of Europe Biomedicine Convention, it is underlined that 'even when the sample is anonymous the analysis may yield information about identity.'[28]

The differences in legal protection between identifiable and non-identifiable data draw attention to a few additional issues. First, the process of de-identification is obviously a crucial point, since this is where the individual concerned definitely loses control over the use of the data.[29] Second, if the legal protection only covers information related to identifiable individuals, no particular protection is offered to the privacy interests of individuals belonging to an identifiable *group*, nor to any donor interest in not contributing to a certain activity. Lack of linguistic interoperability is of course an additional problem that has been repeatedly discussed with regard to the concept of identifiability, both at the domestic and the international level.[30]

Human Material as a Public Resource

Finally, one possible analogy could be made with the concept of public resources or public goods.[31] Since the human genome is often referred to as a common heritage of humanity, this could imply that information on that very genetic heritage should be considered public property. Public resources can be of many different types, such as historical or cultural heritages, natural resources, air and water, public roads and libraries, schools and hospitals. Legal rules pertaining to public resources may thus be quite diverse, but are normally focussed on protection of collective interests rather than individual ones.[32] Decisions on the use of public resources would typically be based on some form of community consent and equitable access. The resources are protected and preserved for future generations and not-for-profit principles are often applied. It is normally understood that public resources should be used for the public good, but this does not necessarily mean that all benefits gained from the use of a public resource are also shared within the community. With regard to human biobanks and genetic data, however, it has been argued that 'benefits *resulting from* the use of human genetic data, human proteomic data or

[28] Explanatory memorandum paragraph 135, with reference to relation to Article 22 of the Convention.

[29] Cf. Article 23 of the Council of Europe Recommendation Rec (2006) 4 on research on biological material of human origin.

[30] Elger and Caplan (2006).

[31] Cf. for example the HUGO Ethics Committee Statement on Genomic Data Bases 2002, Knoppers and Fecteau (2003), and Sheremeta and Knoppers (2007).

[32] Ossorio (2007).

biological samples collected for medical and scientific research should be *shared* with the society as a whole and the international community.'[33]

Examples provided on the possible forms of such benefit sharing include the provision of new diagnostics, facilities for new treatments or drugs stemming from the research; support for health services; and capacity-building facilities for research purposes.

Summing Up the Analogies: The Biobank a Legal Anomaly

Although the analogy with health-related personal data would seem appropriate in many instances, it is equally clear that it does not cover all aspects of research on human biological material. One possible objection to the analogy could be that the information embedded in a sample of human material is in a way both endless and unforeseeable, but with the possibility of digitalising DNA and thus transferring the biological information to a file or document; this particular difference between genetic data and biological material does seem to dwindle.[34] Nevertheless, it is undisputable that data cannot in themselves contaminate our environment or spread diseases threatening public health and safety, nor can they be used as raw material for transplants and products or have the potential to develop into a full human being. Samples of human biological material are not *just* carriers of data, but have traits of several other conceptual legal categories as well.[35] From the regulatory perspective, the complex nature of human biobanks would seem to make them into an anomaly, defying any attempt at a simplified analogy. Accordingly, policy makers regulating human biobanks must find a way to balance this combination of diverse legal analogies.

One of the primary goals in the regulation of research biobanking is often to facilitate *justifiable* use of human biological material, for research purposes. This would serve the public interest in gaining new knowledge and – eventually – improved public health, by protecting the freedom of research and guaranteeing research access to information and biological samples. Equitable access, solidarity and sharing of resources are thus important principles to consider in the regulatory process, which also go well with the concept of human biobanks as public resources. Nevertheless, these principles may sometimes conflict with the interests individual researchers could have in excluding others from access to their research materials for at least a certain period of time, especially with regard to biobanks with rare samples collected by the researchers themselves. It may thus be argued that driven too far, the principle of equitable access could reduce the incitements for certain types of research and create difficulties in attracting sponsors. Not only industry, but also many universities and individual researchers seem to find the protection of intellectual

[33] Article 19(a) of the UNESCO International Declaration on Human Genetic Data (2003).

[34] Rynning (2003a), at p. 116.

[35] See e.g. Sethe (2004).

property rights and financial rewards to be important incentives in their research activities.

The precondition that use of biobank materials must be *justifiable* draws attention to the presumption that research biobanking is arguably in the public interest and to the need for legitimacy. Since the creation and continued existence of large-scale research biobanks is very much dependent on the goodwill and political support of the donors, i.e. the public, it would certainly be unwise to 'jeopardize, for the sake of administrative convenience and short-term research gains, the interests, the wishes, and [...] rights of those who contributed to these resources',[36] thereby also putting at risk the long-term interests of biomedical science.

Public trust in biobank research involving genetic testing is believed to primarily depend on how the use of samples and data is undertaken and communicated, in particular with regard to the areas of 'informed consent, storage, data protection and the degree of anonymity of samples, the communication of study results and, where appropriate, of individual test results.'[37] These privacy issues are further complicated by the difficulties involved in the provision of adequate protection to all donors (including for example minors and unborn children) as well as to their families and other related groups or populations. Issues of confidentiality could also concern the potential access of third parties to samples and data, for different purposes. Even biobanks exclusively set up for research-related purposes could potentially be used as sources of information for example in a criminal investigation.[38]

Irrespective of the need for protection of confidentiality and other privacy rights, the public obviously has additional interests in the appropriate use of human biological material, related to more abstract and evasive moral values, such as our perception of human dignity in a wider sense. If our dignity as human beings and our respect for others could be put at risk by certain uses of human material, this should be taken into consideration and balanced against the public interest in scientific development. The problem is of course to decide which particular moral concerns should be recognised and what weight they should be attributed in the balancing against hopes for improved global public health and well-being. This is also a field where the plurality of moral and religious values will continue to constitute an obstacle to harmonised international or European rules in certain areas of research.

It is clear that human biobanks give rise to many controversial issues that are debated internationally as well as at the domestic level. Areas of controversy may concern for example the type and scope of donor and community consent, the rights of donors to know and not to know individual results, the role and form of ethics review, conditions for access to samples and data, property rights and commercial

[36] Greely (2007).

[37] McNally and Cambon-Thomsen et al. (2004a), at p. 23.

[38] Cf. Council of Europe Recommendation R (92) 1 of the Committee of Ministers to member States on the use of analysis of deoxyribonucleic acid (DNA) within the framework of the criminal justice system. For an account of the use of the Swedish PKU biobank in the investigation following the murder of Sweden's Minister of Foreign Affairs, Anna Lindh, see Wendel (2007), at p. 115.

interests in biobanking, and governance and monitoring.[39] In order to give just a few examples from the international debate, some comments will be provided concerning the relationship between the biological samples and genetic data, the justifiability of genetic exceptionalism and the ambiguity of the term anonymity.

Some Areas of Controversy

Biological Samples Are Not Data

The fact that human biological material has not traditionally been perceived primarily as a carrier of personal data, and is at all events not *only* a carrier of data, has caused uncertainty about the direct applicability of data protection legislation to biobank materials. To the extent that data protection rules are considered applicable, questions also arise concerning the interpretation of such provisions in the particular context of biobanks and the potential conflicts with other rules that could be of relevance.[40]

Not surprisingly, for example the implementation and interpretation of the so-called Data Protection Directive 95/46/EC,[41] with regard to biobank materials and associated data, varies considerably between different Member States of the European Union.[42] Although it would seem clear that personal genetic *data* fall under the Directive, few Member States have taken the position that this applies to the human biological material carrying the genetic information.[43] It is also the opinion of the Article 29 Data Protection Working Party that whereas human tissue samples are sources out of which personal data can be extracted, they are not personal data themselves.[44] The *extraction of information* from the samples therefore constitutes collection of personal data, to which the data protection rules apply, but the collection, storage and use of the tissue samples may be subject to separate sets of rules.

Despite the fact that biological samples are not data themselves, it can still be argued that human tissue should be protected to the same extent as other media carrying sensitive personal information.[45] If different rules are applied to biological samples, as compared with other carriers of personal data, this could lead

[39] Cambon-Thomsen et al. (2007).

[40] Rynning (2003a), at p. 117. See also the Article 29 Data Protection Working Party, Working Document on Genetic Data adopted in March 2004.

[41] Directive 95/46/EC of the European Parliament and of the Council of 24 October, 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data.

[42] Rouillé-Mirza and Wright (2004) at p. 193 f.

[43] As for the case of Denmark, however, see Hartlev (2005), pp. 236–237.

[44] Opinion 4/2007 on the concept of personal data.

[45] See for example the Council of Europe Recommendations mentioned in footnote 23; also the Article 29 Data Protection Working Party, Working Document on Genetic Data adopted in March 2004.

to unwanted and peculiar consequences, for example inconsistencies in the rules pertaining to DNA in digitalised versus natural form. Nevertheless, additional protection would often seem to be called for with regard to other aspects of the use of human material.

Genetic Exceptionalism

One controversial question is whether or not genetic data are actually different from other types of health data, to such an extent as to merit special legal protection of the data or their source, i.e. the human biological material. This kind of so-called genetic exceptionalism is argued in for example the UNESCO International Declaration on Human Genetic Data (2003), where it is claimed that human genetic data have a *special* status, due to the following characteristics:

i they can be predictive of genetic predispositions concerning individuals.
ii they may have a significant impact on the family, including offspring, extending over generations, and in some instances on the whole group to which the person concerned belongs.
iii they may contain information the significance of which is not necessarily known at the time of the collection of the biological samples.
iv they may have cultural significance for persons or groups.[46]

A similar view is held by the Article 29 Data Protection Working Party, referring also to the fact that identification of individuals by the genetic print presents an additional unique nature of genetic data, since 'genetic data are likely to reveal information on several people while making it possible to identify only one of them'.[47] Although particular legal protection is found to be both needed and justified, however, the Working Party points out that one of the first guarantees conditioning the use of genetic data should be to avoid attributing to these data a universal explanatory value.

The primary argument normally brought forward against genetic exceptionalism is that the characteristics of genetic information are by no means unique, but could all be found in different types of other health-related information.[48] In accordance with this line of argument, beliefs that genetic information is exceptional would rather seem to be based on the mistaken idea that our genetic composition determines our future. By responding to this misconception with exceptionalistic regulation on genetic information, policy makers could thus implicitly provide support for genetic determinism and 'the notion that genetics exerts special power over our lives.'[49]

[46] Article 4 (a) of the UNESCO International Declaration on Human Genetic Data (2003).

[47] 2004 Working Document on Genetic Data, p. 4.

[48] McNally and Cambon-Thomsen et al. (2004b), pp. 32–34.

[49] Murray (1997).

In the 25 recommendations on genetic testing presented by a group of European experts, it is argued that 'the sentiment that genetic data are different from other medical information [...] is inappropriate.'[50] Nevertheless, the group of experts acknowledges that 'some genetic information, as part of medical information, has specific dimensions which are not necessarily common to all medical information.'[51] They find that current efforts to establish laws and regulations that apply specifically to genetic testing and data handling are an understandable response to public concerns, but insist that they are 'only acceptable as a stepping stone to more considered and inclusive legal and regulatory frameworks that encompass all medical data and testing'.

It would seem that the justifiability of genetic exceptionalism is partly a question of how this concept is defined, since beliefs about genetic exceptionalism may be of regulatory significance without necessarily being true.[52]

The Ambiguity of Anonymity

Since the question of identifiability could have considerable impact on the privacy protection offered with regard to data as well as biological materials, it is all the more problematic that lack of terminological interoperability in this field continues to prevail and that the definitions adopted are often incomplete. A few examples from well-known European and international soft law instruments illustrate this quite clearly.

In the Council of Europe Recommendation from 2006, biological materials are thus divided into two main categories based on whether they are considered identifiable or not. Identifiable are those biological materials which, alone or in combination with associated data, allow the identification of the persons concerned *either directly or through the use of a code*.[53] If the user of the biological materials has access to the code, the materials are referred to as 'coded', whereas the term 'linked anonymised materials' is applied when the code is under control of a third party and not accessible to the user of the biological material. Non-identifiable materials, in the recommendation also referred to as 'unlinked anonymised materials', are those biological materials which, alone or in combination with associated data, do not allow, with reasonable efforts, the identification of the persons concerned. In the Explanatory Report, a reference is made to the definition of 'identifiable' in Directive 95/46/EC on the protection of personal data. In the terms of this Directive, however, a person can be *indirectly* identifiable for example with reference to 'one or more factors specific to his physical, physiological, mental, economic, cultural or

[50] McNally and Cambon-Thomsen et al. (2004a), pp. 8–9.

[51] McNally and Cambon-Thomsen et al. (2004b), p. 35.

[52] Ample evidence of this is provided e.g. in Kakuk (2008).

[53] Article 3.

social identity', without any use of a code.[54] The question of how this possibility of indirect identification should be interpreted has been subject to endless discussion already with regard to data.[55] Since the possibility of indirect identification would seem even more relevant with regard to human biological material containing DNA – as has been previously pointed out in another Council of Europe document[56] – it is unfortunate that the issue is not pursued in this Recommendation.

In accordance with the terminology used in this Council of Europe Recommendation, anonymous human biological materials and data can thus be either non-identifiable or identifiable, depending on whether they are unlinked or linked to identifying information by the use of a code. This does in a way highlight the ambiguous use of the term anonymous, which in some contexts may be understood to mean merely 'coded' and in others 'non-identifiable.'

The Council of Europe terminology would not seem to have been considered relevant to the definitions recommended by the European Medicines Agency (EMEA), in their note of guidance on definitions for genomic biomarkers, etc. In the EMEA definitions that were finalised during 2007 and came into operation in May 2008, anonymised data or samples do *not* allow for the donors to be identified. Here, genomic data and samples are divided into four categories: 'identified', 'coded', 'anonymised' or 'anonymous'.[57] Whereas this terminology makes an additional distinction between anonymised and anonymous samples, there is still no category for samples that are only indirectly identifiable by *other* means than coding, for example by use of information on the time and place where the sample was collected and various features of the donor. This type of samples or data would not really seem to fit the description of the category 'identified', which refers to samples or data labelled with personal identifiers such as name or identification numbers (e.g. social security or national insurance number) that make them 'directly traceable back to the subject'. Should indirectly identifiable samples then be considered anonymous? 'Anonymisation' in the EMEA guidance refers to the deletion of the link between the subject's identifiers and the unique code of such samples or data as have initially been *coded*, and it is intended to prevent subject re-identification. 'Anonymous' data and samples are defined as never having been labelled with personal identifiers when originally collected, and no coding key having been generated, but it is also made clear that there is no potential to trace anonymous genomic data and samples to individual subjects.

The slightly older UNESCO Declaration on Human Genetic Data (2003) distinguishes between three categories of data, with regard to their degree of

[54] Article 1 a.

[55] See e.g. Romeo Casabona (2004). See also the Article 29 Data Protection Working Party Opinion 4/2007 on the concept of personal data.

[56] Cf. paragraph 135 of the Explanatory Memorandum to the Biomedicine Convention, concerning Article 22.

[57] ICH Topic E15 Definitions for genomic biomarkers, pharmacogenomics, pharmacogenetics, genomic data and sample coding categories. Note for Guidance on Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories.

identifiability: (a) data 'linked' to an identifiable person (i.e. data that contain information, such as name, birth date and address, by which the person from whom the data were derived can be identified), (b) data 'unlinked' to an identifiable person (i.e. data that are *not* linked to an identifiable person, through the replacement of, or separation from, all identifying information about that person *by use of a code*) and, finally, (c) data 'irretrievably unlinked' to an identifiable person (i.e. data that cannot be linked to an identifiable person, through destruction of the link to any identifying information about the person who provided the sample).

Comparing these three documents, adopted by highly influential European and international agents and often referred to, it is surprising to find such diversity in the terminology used. Samples or data that have been coded, and where the user of them does not have access to the key, could thus be defined as 'linked anonymous', 'coded' or 'unlinked', depending on which guiding document is consulted. In the same way, samples or data that are labelled or associated with personal identifiers, such the name or social security number of the person concerned, could be defined as 'directly identifiable', 'identified' or 'linked'.

In addition to this terminological confusion, all three documents lack clarity with regard to the categorisation of samples and data where the person concerned could be indirectly identified by the user, or by somebody else, with reasonable effort. Such indirect identification of donors would not seem too difficult to achieve even in large-scale biobanks.[58]

Varying Strategies in Domestic Regulation: Some Examples from the Nordic Countries

Is There a Nordic Approach to Biobank Legislation?

Before discussing the possibility of harmonised global or European rules for research biobanking, it could perhaps be of interest to briefly consider the differences and similarities found in regulations developed within a more limited geographic area, such as the Nordic countries. The five autonomous nation states of Denmark, Finland, Iceland, Norway and Sweden form one of the oldest and most comprehensive regional co-operation areas in the world, sharing a considerable part of their cultural and historical heritage.[59] The Nordic languages are also closely related, with the one exception of Finnish (but then Swedish has been the second official language of Finland for nearly a century). One particular field of modern day co-operation, dating back more than a 100 years, has been law reform and the drafting of new legislation. The Nordic countries also pride themselves of being unique in

[58] See for example Greely (2007).

[59] For more information on Nordic co-operation, see the Web page of the Nordic Council, http://www.norden.org/start/start.asp.

terms of well-developed population records and other databases, which has made them very well suited for epidemiological research.

Considering this tradition of co-operation and shared Nordic values, there seems to have been surprisingly little regulatory coordination in the areas of health care and biomedical research.[60] There is for example a great variety in the time of introduction, regulatory method applied and material contents of the Nordic laws on topics such as the status and rights of patients, assisted procreation,[61] genetic testing or ethics review of research. The list of differences in approach and timing could be made much longer and include also ratifications of the Council of Europe Biomedicine Convention (Denmark in 1999, Iceland in 2004 and Norway in 2006, while Finland and Sweden are still lacking). Bringing the focus back to the specific area of biobank regulation, however, Iceland here took the lead with the Act on Biobanks that entered into force in January 2002, having introduced the Act on a Health Sector Data Base some years before. Within a period of just a few years, the other Nordic countries all adopted some kind of biobank legislation.

Although it is not possible to provide any comprehensive comparative overview of the Nordic biobank laws and regulations in this context, a few comments could still be motivated in order to illustrate some of the variations seen both in approach and in material rules. It should be noted, however, that revisions of the biobank legislation are taking place in several Nordic countries. In a Norwegian Bill that was passed in June 2008, the Act on Biobanks is incorporated in a new Act on Health Research, which will enter into force at a date to be decided later.[62] In this new version, several provisions are changed in a more liberal direction, in order to facilitate research. Finland would seem to be considering a change of strategy and is now discussing the introduction of more comprehensive biobank legislation.[63] An investigator has recently been appointed to revise the Swedish biobank legislation, which has been subject to a lot of criticism due to a number of different shortcomings.[64] In this context, it is also of relevance that the regulatory landscape surrounding the biobank provisions has changed since the biobank laws were first passed. In Sweden, for example, an Act on Ethics Review of Research Involving Humans entered into force in 2004 and an Act on Genetic Integrity in 2006.[65] Most recently, there is a new Act on Patient Data[66] as well as legislation based

[60] An overview of Nordic law in the field of biotechnology, in the form of tables updated as of April 2005, can be found in the publication Legislation on Biotechnology in the Nordic Countries – An overview, TemaNord 2006: 506.

[61] On the Nordic differences in this field, see Burrell (2006).

[62] *LOV 2008–06–20 nr 44: Lov om medisinsk og helsefaglig forskning (helseforskningsloven)*; see Government Bill Ot.prp. nr. 74 (2006–2007).

[63] Information provided at the Web page of the Finnish Ministry for Social Affairs and Health, http://www.stm.fi/Resource.phx/hankk/biopankki/index.htx.

[64] Terms of reference issued by the Swedish government: Direktiv 2008:71, Översyn av lagen (2002: 297) om biobanker i hälso-och sjukvården m.m.

[65] *Lag (2006: 351) om genetisk integritet*.

[66] *Patientdatalag (2008: 355).*

on Directive 2004/23/EC on human tissues and cells.[67] In all the Nordic countries, the complex relation to other legislation has implications for the applicability and interpretation of the specific biobank regulation.

Type and Scope of Nordic Biobank Legislation

The Nordic countries thus all decided to regulate the use of human biobank materials at approximately the same time,[68] but the legal solutions preferred vary considerably. Iceland chose to introduce as a comprehensive Act on Biobanks, a strategy also adopted in Sweden and Norway, where such acts entered into force in 2003.[69] Denmark and Finland, on the other hand, have so far addressed the biobank issues by introducing complementing provisions in already existing, more general laws. The reasons for this difference in approach could at least partly be found by comparing the coverage in previous legislation of issues related to biobank research and the perceived special problems arising from biobank activities. At the start of the new millennium, both Denmark and Finland already had legislation on ethics review of research as well as on patients' rights.[70] In Denmark, these Acts were complemented with certain biobank-related provisions, but the general data protection legislation had previously been declared directly applicable to biobank samples.[71] In Finland, the revised Act on the Use of Human Organs and Tissue for Medical Purposes was supplemented with new provisions on the collection and further use of human tissue.

Iceland also had legislation on patients' rights and a ministerial regulation on scientific research in the health sector,[72] but still felt that a special Act on Biobanks was needed to regulate certain specific activities. The Icelandic Act on Biobanks

[67] *Lag (2008: 286) om kvalitets- och säkerhetsnormer vid hantering av mänskliga vävnader och celler*, implementing Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.

[68] For some of the early legal debate in the Nordic countries, see e.g.: Nielsen et al. (1996), Arnardottir et al. (1999) and Eriksson (2003). For those familiar with the Nordic languages, more comprehensive analysis of the Danish, Norwegian and Swedish biobank laws can be found in the following works: Hartlev (2005), Halvorsen (2006) and Rynning (2003b).

[69] Swedish Biobanks in Medical Care Act, *Lagen (2002:297) om biobanker inom hälso- och sjukvården m.m.*, in force 1 January 2003 and the Norwegian Act on Biobanks, *LOV 2003–02–21 nr 12: Lov om biobanker (biobankloven)*, in force from 1 July 2003.

[70] See the Finnish Act on the Status and Rights of Patients, *Lag om patientens ställning och rättigheter 17.8.1992/785* and the Danish Act on the Legal Status of Patients, *Lov om patienters retsstilling LOV nr 482 af 01/07/1998* (later incorporated in the 2008 Health Act, *Sundhedsloven*); the Danish Act on Ethics Review of Scientific Research, *Lov om et videnskabsetisk komitésystem og behandling af biomedicinske forskningsprojekter LBK nr 69 af 08/01/1999* and the Finnish Act on Medical Research, *Lag om medicinsk forskning 9.4.1999/488.*

[71] See report from the Danish Ministry of Interior and Health (2002) Redegørelse om biobanker, pp. 49–52.

[72] The Icelandic Act on the Rights of Patients No. 74/1997 and the Icelandic Regulation on Scientific Research in the Health Sector No. 552/1999.

is in fact the only one of the Nordic biobank laws that exclusively deals with *long-term* research biobanks, where samples are to be kept for more than 5 years. It can be assumed that the heated debate on the Icelandic Health Sector Data Base Act and the plans of deCODE Genetics to collect blood samples from all of the Icelandic population had some influence on this legal development.[73] Icelandic research biobanks of a more temporary character are still governed by the rules on scientific research and the processing of personal data.[74]

A different point of departure is chosen in the Biobank Acts of Norway and Sweden, where the choice of comprehensive legislation would seem to have been based primarily on a wish for uniform and accessible rules to govern the majority of research biobanks as well as banks for diagnostic or treatment purposes. Whereas the original Norwegian Act is applicable to all such biobanks, however, the Swedish Act covers only samples from identifiable donors, and only banks that have been set up within the professional activities of a health care provider, thus excluding for example biological materials that have been collected directly by a pharmaceutical company or a research institution, purely for research purposes.[75] Provided the samples in such biobanks can be traced to an identifiable donor, however, the research would still fall under the Act on Ethics Review and be subject to the same consent requirements, but a number of additional safeguards laid down in the Act on Biobanks would not apply. Needless to say, this distinction, which was criticized even before the Act was passed, has created considerable problems related to interpretation and implementation of the Swedish rules. Furthermore, no criteria for the crucial concept of donor identifiability have been presented.

The comprehensive Icelandic, Norwegian and Swedish Biobank Acts all contain special provisions regarding registration and monitoring of biobank activities and in particular the Icelandic legislation closely regulates the rights and administrative duties of the 'biobank licensee'. The Swedish and Norwegian Biobank Acts also prescribe certain restrictions with regard to international transfer of biobank material, even within the EU.

Issues of Consent and Withdrawal

At first sight, the legal prerequisites related to the collection or use of human biological material for research purposes may not seem very divergent. The main rules in all the Nordic countries thus include requirements for ethics review and informed donor consent, but with regard to use for new purposes of samples already banked, the rules show a wider variation. It should also be noted that since the Icelandic Act is aimed exclusively at long-term biobanking, the informed consent required for collection and storage under this Act may be quite broad, or even what is called 'open consent', indicating that the aims, purposes, methods, etc. of the future projects for

[73] Arnardottir et al. (1999).

[74] See Articles 2 and 15 of the Act on the Rights of Patients No. 74/1997.

[75] If the samples in such biobanks can be traced to an identifiable donor, they would still fall under the Act on Ethics Review and would thus be subject to the same consent requirements, etc.

which the samples may be used, are unknown at the time when they are collected.[76] When the samples are later used in research, no additional consent is needed.

The other Nordic countries would not seem to accept the kind of open consent used for Icelandic research involving samples from long-term biobanks, but this does not mean that a fully informed and specific consent will always be a necessary prerequisite for research on biobank materials. Although consent is formally the default requirement when banked materials are to be used in a project for which the donor's specific consent has not already been obtained, all the Nordic countries provide exemptions from this requirement. In Denmark and Sweden, as in Iceland, the competent ethics committee may thus allow the use of biobank materials for new research-related purposes without consent, under certain circumstances. In Norway, such exceptions must also be authorised by the Ministry of Health and Care Services and in Finland by the National Authority for Medicolegal Affairs. The prerequisites for the exemptions also vary somewhat between the countries.

In this context, it should be noted that all the Nordic countries, except Sweden, view the preservation of biological samples from patients, for purposes related to their own future health care needs, as a more or less integrated part of the medical record keeping, which is carried out independent of the patients' wishes.[77] Since such samples may prove to be of interest also to researchers, the rules pertaining to further use could in practice result in research use without any consent at all. In Denmark, a special opt-out register has been introduced, where patients can register their wish not to have their samples in clinical biobanks used for other purposes than those related to their own health care.

As a contrast, the Swedish Biobank Act provides a good illustration of the difficulties involved in applying the *same* consent requirements to biobanking for health care purposes as to banking for research purposes. In order to meet reasonable prerequisites for banking of biological samples in view of research use, the consent requirements are unusually strict from the health care perspective. Explicit, specified informed consent is thus formally required also for the preservation of samples for purposes related to the future health care of the donor (with the exception of routine samples that are only preserved for a shorter time, normally not more than 2 months). At the same time, the 'informed consent' required for the *storage* of clinical samples also in view of future research is in fact so unspecific that it will normally be quite insufficient as consent to the participation in a future research project. The administrative burdens placed on health care providers thus seem somewhat disproportionate. In practice, however, the Swedish health care providers have adopted a pragmatic approach to this demanding opt-in system and actually apply what is in principle an opt-out system, where the patient has to send in a so called no-thank-you-counterfoil if he or she does not wish the sample to be stored.[78] Even

[76] Helgasson (2004).

[77] See, for example, Section 11 of the proposed Norwegian Act on Health Research and the report from the Danish Ministry of Interior and Health (2002) Redegørelse om biobanker, pp. 195–196.

[78] An English version of this counterfoil can be accessed at the biobank webpage of the Swedish Association of Local Authorities and Regions, http://www.biobanksverige.se/getDocument.aspx?id=79.

so, Sweden would seem to be the only Nordic country where a patient has an unconditional right to have a biobank sample destroyed or de-identified even when it is being kept solely for the secure health care of the donor himself or herself.

With regard to samples intended for *research* purposes, however, all the Nordic countries except Denmark[79] allow donors to withdraw their consent at any time and have the samples destroyed or at least de-identified.[80] In Norway, the donor may even have the information extracted from the sample erased.

Access and Benefit Sharing

Whereas Denmark considers the data protection legislation to be directly applicable to biobank samples and the Norwegian biobank definition includes data that are associated with the biological material, the other countries apply more separate sets of rules to data and biological material. At least in Sweden, this has direct implications also for the accessibility of the materials. Although researchers are able to invoke their constitutional right of access to data in the files and documents of public agencies and institutions (albeit subject to applicable privacy restrictions),[81] there is no corresponding right of access to samples stored in biobanks set up by such agencies, even if the donors were to accept it.[82] In the case of digitalised DNA, however, the rules pertaining to data would of course apply.

Neither would any of the other Nordic countries seem to provide legal guarantees for equitable research access to biobank samples. The fundamental prerequisite that biobanks should be used in ways that are conducive to the public good, however, is established in the introductory sections of both the Icelandic and the Norwegian Biobank Act.

The concept of biobanks as shared resources is not completely absent in the Swedish legislation either. The fact that a biobank may constitute a valuable public resource is for example referred to in the *travaux préparatoire* in relation to the provision regulating the closing down of a biobank, that is no longer considered significant to the purpose for which is was established.[83] Authorisation to close down the bank and destroy the samples must thus be sought from the National Board of

[79] According to the position of the Danish National Committee for Biomedical Research Ethics, donors should not have the right to have their samples and data removed from use in an ongoing research project, whereas they should otherwise be allowed to have their banked samples and data removed; see the Committee yearbook 2003 (Den Centrale Videnskabsetiske Komités Årsberetning 2003), p. 37 f.

[80] Section 7 of the Icelandic Biobank Act; Section 7 of the Finnish Act on the Use of Human Organs and Tissue for Medical Purposes and Section 14 of the proposed Norwegian Act on Health Research.

[81] This general right of access to official documents is regulated in the Freedom of the Press Act, and it covers also documents in for example public universities and hospitals; see Rynning (2004), p. 383.

[82] Rynning (2003a), p. 116f.

[83] Government Bill 2001/02:44 Biobanks in Health Care, pp. 54–55.

Health and Welfare, who will consider if there is no public interest in preserving the specimens. The Act on Biobanks also offers a possibility for researchers who are refused access to the samples in a biobank, to have the refusal (re)considered by the National Board of Health and Welfare, but the opinion of the Board is not binding to the biobank principal.

All the Nordic countries in principle support the standard of non-commercialisation of human biological material as such and explicitly prohibit transactions of human material in view of financial gain. Although this principle is by no means without exceptions,[84] the laws do not address the possibility of benefit sharing. The area of lawful financial incitements for the donation or sharing of biobank samples is thus a matter of interpretation, but would seem to be rather limited outside the scope of actual cost coverage. When the biobank sample is turned into a product or some kind of research results, however, the principle of non-commercialisation no longer applies. Unfortunately, the relevant criteria defining such transition remain unclear.[85]

The Challenge of International Harmonisation

These brief comparative comments illustrate how different the legal approaches to biobank issues can be, and how the focus and strategies applied in the regulation of biobanks may vary quite widely, even within a comparatively homogenous region such as the Nordic countries. In the global and even the European perspective, harmonisation projects must be expected to involve more complex challenges, considering the existing diversity of cultural and religious values as well as the pluralism of legal traditions. In this context, questions also arise concerning the regulatory competency of different international or supra-national organisations, and the regulatory tools available.

Regulatory Tools and Competency

Hard Law and Soft Law

When different types of regulation and governance are discussed, one distinction often made is the one between formally binding hard law regulation and various types of so-called soft law, in the form of codes of conduct, declarations, resolutions, recommendations, guidelines, policy documents, etc.[86] Even though soft

[84] For example in Sweden, exceptions apply to blood, hair, breast milk, teeth, de-identified embryonic cell lines, as long as they are not already part of a biobank; see Chap. 8, Sect. 6 of the Act on Genetic Integrity.

[85] Rynning (2003a), pp. 103–105; Halvorsen (2006), pp. 219–220.

[86] This section is based on Rynning (2009).

law regulation is normally classified as rules that are not legally binding as such, the boundary between hard law and soft law is not distinct and the two types of regulation often interact in different ways. Soft law instruments may thus have certain – indirect – legal effects and are aimed at and may produce practical effects.[87] Sometimes soft law can be viewed as a transitional mode of regulation, a precursor to binding legal instruments, but it may also be used as an independent, alternative steering mode, conveying power to actors that have only limited influence in traditional regulatory processes.[88] Soft law regulation can be introduced also in areas where 'the legal competence [of the regulatory body] is weak or nonexistent',[89] and is thus a tool available to non-governmental organisations[90] as well as other actors with limited regulatory powers, for example the OECD. The status of soft law documents will thus be dependent on context as well as time. Guidelines issued for example by a ministry or by a competent public authority are likely to have a formally stronger standing than a code of conduct issued by a professional organisation, but the latter type of guideline may become indirectly binding, if considered to express the professional standard required by law, i.e. 'good practice', or if it is explicitly referred to in binding regulation. In the area of public international law, soft law documents may also be used as tools for the interpretation of binding instruments.

Although questions may well be raised concerning the democratic legitimacy of soft law,[91] such instruments also have certain advantages. Soft law is thus considered to leave more room for flexibility and rapid reactions and is believed to be particularly useful 'when dealing with complex and diverse problems that are characterized by uncertainty'.[92] This type of regulation is therefore often found in areas of human rights and environment. However, since soft law in itself does not provide any legal sanctions, such regulation alone is not sufficient where important interests must be guaranteed appropriate judicial protection.

International Regulation

The fact that it is primarily the duty of the nation states to provide an appropriate legal framework for protecting the human rights of individuals and other important interests related to the private or the public sector, by no means excludes the possibility of international regulation. In areas where harmonisation is called for, the introduction of international norms could on the contrary be highly desirable as tools

[87] Senden (2005).

[88] Mörth (2004b), at p. 198.

[89] Frykman and Mörth (2004), at p. 163.

[90] Consider for example the impact of the World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (adopted by the WMA General Assembly in 1964, revised in 1975, 1983, 1989, 1996 and 2000).

[91] Frykman and Mörth (2004).

[92] Mörth (2004a), at p. 3.

for both voluntary and mandatory adjustments of domestic laws. The appropriate level of the regulation is a question of legal competency, but also of suitability and principles of subsidiarity. However, in particular where a certain topic or issue does not fall within the competency of any supranational organisation, the development of *binding* international rules obviously presupposes the existence of consensus.

At the global level, a number of normative documents in one way or another addressing biobank-related issues have been adopted by inter-governmental bodies, for example the WHO 1998 Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetic Services, the UNESCO Declaration on the Human Genome and Human Rights (1997) and the UNESCO Declaration on Human Genetic Data (2003). A more recent document in this the field is the OECD 2008 Draft Guidelines for Human Biobanks and Genetic Research Databases. All these documents, however, belong to the area of soft law and accordingly do not have any formally binding status.

At the European level, there are two particularly important actors of relevance to the regulation of research biobanking: The Council of Europe and the European Union. While the Council of Europe is without doubt the most important and influential European body with regard to the protection of human rights, the European Union – with its primary focus on economical cooperation and development – is in many ways a more powerful institution. Even so, since the EU only has limited regulatory competency in areas of health care, research ethics and human rights, the powers of this supra-national organisation would not seem to fully encompass the legal issues arising from research biobanking.

The Council of Europe

The Council of Europe quite early took an interest in the use of human biological material, both as a source of information and as material used for transplantation and other applications. Recommendations from the Committee of Ministers in the late 1970s include topics such as harmonisation of rules on the taking and use of human substances for transplantation, as well as international exchange and transportation of human substances.[93] With the growing advances in genetics, several recommendations on the use of genetic analysis and genetic screening for different purposes were adopted in the early 1990s,[94] followed by a recommendation

[93] Recommendation R (79) 5 of the Committee of Ministers to member States concerning international exchange and transportation of human substances and Recommendation R (79) 5 of the Committee of Ministers to member States concerning international exchange and transportation of human substances.

[94] Recommendation R (90) 13 of the Committee of Ministers to member States on prenatal genetic screening, prenatal genetic diagnosis and associated genetic counselling, Recommendation R (92) 1 of the Committee of Ministers to member States on the use of analysis of deoxyribonucleic acid (DNA) within the framework of the criminal justice system and Recommendation R (92) 3 of the Committee of Ministers to member States on genetic testing and screening for health care purposes.

on human tissue banks in 1994.[95] Not until 2006, however, was a recommendation adopted that explicitly addresses issues related to the use of human biological material in research.[96] All these recommendations belong to the area of soft law, as opposed to the Council of Europe Conventions, which are formally binding to the ratifying parties. In this category there is not only the firmly established European Convention on Human Rights and Fundamental Freedoms (ECHR 1950), which provides both basic principles and a procedural framework for enforcing the rights, but there is also the Convention on Human Rights and Biomedicine (1997), with the Additional Protocol concerning biomedical research (2005). Although the Biomedicine Convention is not as widely ratified as the ECHR,[97] and lacks an adequate system for enforcement, it still has had considerable impact on the legal development both within Europe and at the global level.[98]

When it comes to research biobanking and the distinction between materials collected for a specific project and those stored for future research, however, it is not altogether easy to determine the outcome of the multi-layered set of rules provided by the combination of legally binding provisions in the ECHR, the Biomedicine Convention and the Protocol on Research, with the 2006 Recommendation.[99] The explanatory memorandum to the Protocol on Research states that this instrument is not applicable to the removal and storage of human material for *future* research, whereas Article 11 of the Recommendation on biological material prescribes that the Protocol *should* be applied. Since for example the consent requirements of the Protocol are more strict and detailed than those of the Recommendation, it becomes unclear what the applicable requirements really are. On the question of how to balance the donors' right to know with their right not to know of information collected about their health, uncertainty also prevails. References to the general provisions in Article 10 of the Biomedicine Convention, indirectly made in Article 25 of the Recommendation via article 26 of the Protocol on Research, do not provide any real guidance.

Despite its shortcomings, which include also the inadequacies mentioned earlier with regard to the definition of non-identifiable data, the Recommendation on research on biological material of human origin is still an important document, as the first official and comprehensive European instrument on this topic. Nevertheless, due to its vagueness and the lack of comprehensive examples, doubts have been

[95] Recommendation R (94) 1 of the Committee of Ministers to member States on human tissue banks. The definition of human tissue in this recommendation is very narrow, however, thus covering 'all constituent parts of the human body, including surgical residues but excluding organs, blood and blood products as well as reproductive tissue, such as sperm, eggs and embryos. Hair, nails, placentas and body waste products are also excluded.'

[96] Recommendation Rec (2006) 4 of the Committee of Ministers to member states on research on biological materials of human origin.

[97] At present (December 2008), the Biomedicine Convention has been ratified by 22 member states of the Council of Europe, although signed by more than 30.

[98] Roucounas (2005) and Gadd (2005).

[99] See for example Nys (2008).

raised as to the usefulness of this Recommendation to drafters of binding biobank regulations.[100]

The European Union

Despite the existence of several legal EU instruments that concern certain aspects of biobanking, there is none specifically addressing research biobanking. To the extent that biobank materials are understood to constitute carriers of personal data, certain activities must thus comply with the requirements of Directive 95/46/EC on the protection of personal data. When biobank research on human biological materials lead to new inventions, Directive 98/44/EC on the legal protection of biotechnical inventions could be relevant. If biological samples are used in pharmaceutical trials, there is Directive 2001/20/EC on the implementation of GCP in the conduct of clinical trials to consider, and experiments aimed at using biobank materials or products made of such materials for human application would fall under Directive 2004/23/EC on human tissues and cells, or Regulation (EC) No. 1394/2007 on advanced therapy medicinal products. There is also a very recent proposal for a Directive on standards of quality and safety of human organs intended for transplantation.[101]

All these legal instruments are in one way or another related to EU competency topics such as the free movement of goods and services, consumer safety or public health.[102] As already mentioned, the more specific areas of national research policies and biomedical ethics do not as such fall within the lawmaking competency of the EU, unless it could be successfully argued that harmonisation is necessary for the development of 'a single research area', as a part of the internal market.[103] Indeed, all the aforementioned documents do in fact to some extent touch upon also for example requirements of consent, privacy and ethics review, thereby illustrating the complexity of EU legal development. Even so, it is still unlikely that European consensus could be reached on the more controversial issues related to policies for research involving human subjects or human biological material. In this field, the EU must therefore primarily rely on alternative means of governance to

[100] Harmon (2006).

[101] Proposal for a Directive of the European Parliament and of the Council on standards of quality and safety of human organs intended for transplantation, presented by the Commission December 12, 2008.

[102] They are thus based on Articles 95 or 152 of the EC Treaty. Even such a human rights inspired document as the Data Protection Directive thus has the *primary* aim of facilitating the free flow of personal data; see Recital 8 of the Directive.

[103] Cf. Hervey and McHale (2004), pp. 238 and 281, with reference also to Articles 163 and 164 EC Treaty. In recently adopted Council Conclusions on The Launch of the 'Ljubljana Process', it is declared that 'Europe now needs to develop a common vision and effective governance of the European Research Area (ERA).' See outcome of proceedings Competitiveness Council of 29–30 May 2008.

influence the policies developed in research biobanking, for example so-called open coordination and funding policies, etc.[104]

The advisory body called the European Group on Ethics in Science and New Technologies (EGE), which expresses opinions and adopts recommendations on various issues, can also be regarded as a means of indirectly influencing the policies of Member States. The opinions submitted by the EGE include topics such as human tissue banking and umbilical cord blood banking, as well as research involving human embryonic stem cells,[105] and the group has also addressed issues related to the patenting of products or other inventions based on human biological material.[106] Although the function of the EGE is to provide expert advice to the European Commission, the opinions submitted are of course considered also by various domestic bodies in the Member States.

Addressing the Regulatory Challenges

Human biological material *combines* a number of powerful characteristics, which in different ways distinguish it from other research materials. It is thus an important source of personal data, but at the same time constitutes an extraordinary type of raw material that can be used in its original form or processed into different types of products, and may under certain circumstances even be developed into new human beings. Needless to say, balancing the various and highly important interests concerned by research activities involving such materials is no simple task. It would be unrealistic to expect that an appropriate balance could be achieved without the revision and re-consideration of several less successful attempts, in a process based on extensive and serious public debate.

Research biobanks come in many forms and shapes and are sometimes closely linked to biobanks set up for other purposes. The unlimited potential for multiple use, new use and cross-use of different types of biobank material is another reason for the difficulties involved in finding *the* appropriate set of rules. From a very narrow regulatory perspective, it would certainly be easier if the various types of biobanks could be clearly distinguished from each other and the different uses kept separate, but this is not the reality that has to be dealt with. Therefore, the diversity of biobanks and their potential uses make it very important to be clear about

[104] Hervey and McHale (2004), at p. 239 f, 412 ff.

[105] Opinion n°11 – 21/07/1998 – Ethical aspects of human tissue banking, Opinion n°12 – 23/11/1998 – Ethical aspects of research involving the use of human embryo in the context of the fifth framework programme, Opinion n°19 – 16/03/2004 – Ethical aspects of umbilical cord blood banking and Opinion n°22 – 13/07/2007 – The ethics review of hESC FP7 research projects.

[106] Opinion n°2 – 12/03/1993 – Products derived from human blood or human plasma, Opinion n°3 – 30/09/1993 – Opinion on ethical questions arising from the Commission proposal for a Council directive for legal protection of biotechnological inventions, Opinion n°8 – 25/09/1996 – Ethical aspects of patenting inventions involving elements of human origin and Opinion n°16 – 07/05/2002 – Ethical aspects of patenting inventions involving human stem cells.

the intended scope of different provisions suggested and adopted. Without a clear and consistent terminology, it will remain difficult even to discuss the alternative solutions available.[107]

The international nature of biomedical research undeniably provides a strong incentive for harmonisation of the rules pertaining to research biobanking, but here the complex balancing of diverse interests is further complicated by the plurality of religious, cultural, social and legal traditions. It is unlikely that all such differences could be overcome even in the long-term perspective, but some degree of regional or even international consensus could certainly be hoped for with regard to less controversial areas and issues. It is therefore an important task to identify those areas of consensus and explore the potential for further development of harmonised norms. One indispensable tool in the search for acceptable uniform standards is the comparative research performed in numerous European projects, primarily or partly aimed at finding ways to overcome different regulatory problems in research biobanking.[108] Although the field of biobank research seems to defy any attempt at simple analogies, it is clear that the application of more sophisticated analogical reasoning will still be valuable in the regulatory process.

Continuous interaction between developing soft law and hard law instruments, based on comparative and multi-disciplinary research as well as extensive public debate, is arguably the only way forward in this highly complex area of regulation. It should also be openly recognised that the regulation of research biobanking must be perceived as an ongoing step-by-step process, rather than a problem that will shortly be solved once and for all. In this process, a certain degree of diversity in domestic regulation will provide valuable opportunities to explore different models and approaches and may accordingly be an advantage in the long-term perspective.

The participation of biomedical scientists in the development of adequate standards for biobank research is of course essential. In the short-term perspective, however, life science researchers and biobank principals will have to accept that certain legal restrictions and administrative inconveniences may delay their work, cause additional costs and occasionally even prevent promising research. These are the implications of democracy, where the best interests of the public can only be served by a careful and independent balancing of the freedom of research against other fundamental rights and values.

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[107] Elger and Caplan (2006).

[108] In addition to the project behind this book (Mapping the language of research biobanks), see for example projects such as ELSAGEN (Ethical, Legal and Social Aspects of Human Genetic Databases, http://www.elsagen.net), GeneBanC (Genetic bio and dataBanking: Confidentiality and protection of data, http://www.genebanc.eu), PRIVILEGED (Privacy in Law, Ethics and Genetic Data, http://www.privileged.group.shef.ac.uk), and BBMRI (Biobanking and Biomolecular Resources Research Infrastructure, http://www.bbmri.eu).

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Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use

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Proposal for a Directive of the European Parliament and of the Council on standards of quality and safety of human organs intended for transplantation, presented by the Commission December 12, 2008 (COM(2008) 819 final)
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Opinion n°22 – 13/07/2007 – The ethics review of hESC FP7 research projects
Opinion n°16 – 07/05/2002 – Ethical aspects of patenting inventions involving human stem cells.

The Council of Europe

European Convention for the Protection of Human Rights and Fundamental Freedoms (1950, ETS no. 005)
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Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (1997, ETS no. 164)
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Recommendation R (94) 1 of the Committee of Ministers to member States on human tissue banks

Recommendation (97) 5 of the Committee of Ministers to Member States on the protection of medical data
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