Biotechnology and Genetic Engineering Reviews - Vol. 25, 429-452 (2008)

The Ethics of Research Biobanking: A Critical Review of the Literature

KLAUS HOEYER*

University of Copenhagen, Department of Public Health, Unit of Health Services Research, Oester Farimagsgade 5, Building 15, DK-1014 Copenhagen, Denmark

Abstract

Human tissue has been stored and used for research on a regular basis for more than 80 years. During the 1990s, collections of human tissue suddenly became framed as ethical problems in a process reflecting developments in genetic research intertwined with developments in patient rights and steps towards increased commercialization of research. This review describes the process of framing tissue storage as an ethical problem and the solutions proposed in the process. It gives an overview of the academic debate and relates this debate to empirical studies of donor attitudes and interests. It points to the clear discrepancy between the concerns of donors, legislators and ethicists. The academic debate and legislatory action tend to focus on informed consent, and most of the concerns that donors have remain unattended to.

Introduction

For more than 80 years tissue has been derived from human bodies, stored, distributed and used for therapeutic, educational, forensic and research purposes as part of healthcare routine in most western countries. Gradually such collections have become known under various names such as biobanks, biolibraries, tissue repositories, genetic databases, or DNA banks.[1] In tandem with increased scientific appreciation of their

[1] A fierce battle is being played out concerning the appropriate vocabulary for the tissue collections as well as the people from whom the tissue derives, but in this review the terms 'biobank' and 'donor' are chosen when no specific reason to use other terms is at stake because they are the most common in use and cover most aspects.

To whom correspondence may be addressed (k.hoeyer@pubhealth.ku.dk)

Abbreviations: DNA: Deoxyribonucleic acid, HSD: Health Sector Database, PCR: polymerase chain reaction

worth, during the 1990s such collections began being framed as ethical problems. After having been associated with dull routine for almost a century, the interest in biobanks has exploded – triggering several hundred academic articles as well as a number of books and edited volumes.[2] Despite some media reports claiming that all this interest is a reaction to the disclosure of previously clandestine biobanking practices, those with practical experience of biobanking know that tissue storage in general was never secret. Previously, biobanks were simply not viewed as phenomena deserving all this interest. This article reviews the process through which research biobanks became viewed as ethically problematic (leaving aside debates about therapeutic, forensic and diagnostic biobanks). It seeks to provide an understanding of the driving forces of this tendency to discuss biobanks in the language of ethics and to question its implications. What has suddenly made research biobanks into *ethical* challenges? What type of ethical problem are they now seen to constitute? And how well does the current ethical framing address the concerns that donors might have?

The short version of the argument unfolded below runs as follows. During the 1990s the tissue contained in the biobanks was gradually "personified" in a process involving three interrelated driving forces relating to developments in 1) genetics, 2) the politics of patient rights and organizational liability, and 3) commercialization of research. These driving forces played out differently in various national contexts, but the result was remarkably similar in terms of organisational responses as well as academic commentary. A diffuse sense of anxiety with respect to biobanks emerged in many places but everywhere it was addressed with the same organisational *solution*: the donor should give informed consent. In a sense, informed consent helped demarcate what counted as legitimate disagreements concerning the ethics of biobanks; it became the lens through which the "problem of biobanking" was viewed. I will argue that contrary to the assumptions underlying most academic debates about ethics, there is no reason to believe that the new emphasis on informed consent in the field of biobanking was merely an effect of rational ethical analysis. On the contrary, academic debate in this field is part of a complex political game (Lindblom, 1959; March and Olsen, 1976; Weiss, 1986). This game has transformed national legal frameworks for some of the most costly future research infrastructures in the field of medicine. If we critically assess the wide range of concerns aired in the literature and the available knowledge about donors' concerns, informed consent is an inadequate solution. Therefore, I conclude, it is time to move the debates beyond informed consent and to critically assess what can be done to make biobanks into trustworthy institutions of long-term social durability

The article begins with examples of how biobanks became objects of increased scientific and economic expectations during the 1990s in some western countries, and how these expectations were accompanied by a diffuse ethical anxiety and a sudden demand for the use of informed consent in relation to tissue storage. The following section outlines the main themes from the academic debate about informed consent.

[2] See, for example, Árnason *et al*. (2004); Dabrock *et al*. (forthcoming); Häyry *et al.* (2007); Laurie (2002); Petersen (2005); Petersen and Gottweis (2008); Solbakk *et al*. (2008); Sutrop (2004); Tutton and Corrigan (2004); Waldby and Mitchell (2006); Weir (1998); Weir and Olick (2004); Youngner *et al*. (2004).

Then follows a brief introduction to what we know about donors and their interests. This is followed by a short discussion of the shortcomings of this literature, and in conclusion it is highlighted how donor concerns are poorly addressed through the current focus on informed consent and the need to address this mismatch is discussed.

A sense of anxiety: the birth of an ethical problem

At first glance, the storage of human tissue has a long, monotonous history; however, it cannot be taken for granted that those responsible for the collections, and those from whom samples derive have considered the stored entities in the same way throughout the years. For years the material kept in freezers and paraffin wax was most likely viewed as a type of waste, rather than as part of people's bodies (Clarke, 1995; Morgan, 2002). In the early years of tumour banking, it was even discussed whether a cancerous tumour was a *foreign object* rather than mutated cells. The material removed during surgery was hardly seen as integral to the dignity of the person from whom it derived: the samples primarily represented cancers rather than persons. Similarly, the material collected for cardiovascular research was probably mostly taken to represent blood lipid levels rather than persons. Other tissues, such as placentas, have been shown to have very different meanings around the world and over time (Jenkins and Sugarman, 2005). In short, the basic understanding of what is stored in a biobank cannot be taken for granted. In fact, even in relation to current biobanking it is questionable whether everybody agrees about *what* it is that is stored in the freezers, and individual donors might hold several contradictory views depending on the context in which they are asked (Hoeyer, 2004). Perceptions of tissue and its ethical status are dynamically changing with context and over time, and changing problematizations of research biobanking must be understood with this premise in mind.

In the late 1980s and early 1990s advances in genetic research, in particular the invention of the Polymerase Chain Reaction (PCR) technique, in combination with new information technology made it possible to construct new research programmes on even very small amounts of available genetic material (Mackenzie, 2003; Rabinow, 1996). Concurrently, medical research on tissue acquired an altogether different outlook and population-based genetic research became feasible on a totally new scale. Some biobanks now began also to be known as genetic databases. It has been said a number of times that it was the potential for new uses of old samples that gave rise to the emergent ethical concerns about informed consent (Ashcroft, 2000). However, we should remember that for many years biobanks had been used for heterogeneous and unplanned purposes without instigating this type of debate.[3] It cannot have been new uses as such that raised the awareness of the problem; it is more likely that it was genetics which triggered the emergent sense of ethical anxiety (Jeffers, 2001).

Genetics has a troubled history. Affiliated with the eugenic movement and surrounded by grand hopes and fears typically presented in the media as relating to the "Book of Life", genetics has occupied a special role in the history of medicine (Keller, 2000;

[3] For example, a database constructed for nutrition research was used to confirm the relationship between human papilloma virus and cervical carcinogenesis (Kjellberg, Wang, Wiklund, Edlund, Angstrom, Lenner et al. 1999)

Koch, 2004; Lindee *et al.*, 2003; Novas and Rose, 2000). To many, DNA has come to represent the essence of the person, and a telling title of one of the early ethical commentaries on biobanking illustrates how this thinking was imported into the tissue issue: "Persons as Sources, Samples as Persons?" (Knoppers & Laberge, 1995). Stored samples were no longer recycled hospital waste: they had come to represent persons by proxy (Beskow, *et al.*, 2001). If the use of stored tissue for genetic research had to become debated one way or another – the question remained how? What type of problem did it constitute?

The framing of the problem has followed different national trajectories reflecting different legal and bureaucratic institutions as well local historical events.[4] With limited academic attention, various European organizations formulated guidelines concerning tissue storage at an early stage beginning with the Council of Europe's work in the 1970s and 1980s (Tatarenko, 2006). However, not even the researchers establishing biobanks seem to have known these guidelines. In many ways US ethicists were the first to point to biobanks as potential *ethical* problems in a way that instigated widespread organizational response from biobank researchers. In 1995 two independent reports sponsored by federal authorities proposed much tighter federal regulation – and they encountered strong reactions among pathologists, probably partly because they were misattributed to NIH as official guideline proposals (Stephenson, 1996). The reports were written in the context of increasing emphasis on patient rights and issues of organizational liability in American healthcare in general (Rothman, 1991) and though stimulated by concerns over genetic uses of stored tissue, they both encircled the *rights of donors* as their key concern. Informed consent was already made the corner stone in the battle of the patient rights movement as it could be presented as a solution to almost opposite problems for conflicting stakeholders (from the patients' viewpoint is was expected to enhance patient autonomy; from the perspective of the healthcare organizations it helped avoid litigation in an increasingly costly system of tort). The framing of informed consent as a necessary solution to the diffuse problem of genetic biobank research was supported by an event outside the US.

In 1996 two physicians established a company called deCODE Genetics. They had a plan: to establish three related databases in Iceland: 1) the Book of Icelanders containing complete genealogies of the Icelandic population from the settlement to present day, 2) the Health Sector Database (HSD) containing electronic healthcare data and medical records from 1915 onwards, and 3) a genetic database containing blood samples and extracted genetic data from everybody consenting to donate a sample (Merz *et al.* , 2004; Potts, 2002). The Icelandic government saw the potential in attracting research resources and skilled jobs to the country. Furthermore, through HSD the original plan would imply private sponsorship for the establishment of an electronic medical record. The collection of DNA samples would rely on informed consent and determine research participation, whereas enrolment into the HSD was planned to rely on presumed consent as for record keeping in general. Following a parliamentary process the company was eventually granted the right to establish all three databases (Hodgson, 1998). It was a grand scheme and it did not pass without intense public debate (Pálsson and Harðardóttir, 2002). Some local protest evolved,

[4] It is beyond the scope of this review to analyse the various legal and organizational documents (for overviews in this field see, e.g., (Deschênes & Sallée, 2005; Gibbons, 2007; Helgason, 2007; Kaye, 2007; Knoppers, 1999; Godard, Schmidtke, Cassiman & Aymé, 2003; Kapp, 2006).

but during the debates public support grew (Korts *et al.*, 2004), and the majority of the population is still recorded as being in favour of the endeavour (Árnason and Simpson, 2003). Today, one third of the population has donated samples for the database and despite a general economic setback, the company has attracted huge international investments (Pálsson, 2007). Internationally, however, the plan spurred everything but positive reactions.

Iceland quickly became inundated with anthropologists, sociologists, ethicists and scientists eager to comment on deCODE. The nature of international criticism differed; however, the majority of protestors focused their concern on the same issue: the reliance on presumed consent for HSD enrolment. Almost everybody agreed that *informed* consent would have been in place for genetic research. Interestingly, it all relied on a misunderstanding. Participation in the genetic research database *was* planned to rely on informed consent; only participation in the HSD was planned to rely on presumed consent. The international commentators did not seem to understand that deCODE was planning to establish three separate databases and that the genetic database would determine research participation and rely on informed rather than presumed consent. The reason for using presumed consent for the HSD was that if only some patients were transferred to electronic record keeping, the state would still have needed to establish an alternative electronic patient record for those opting out, and the public benefits would thereby have been smaller (Potts, 2002). Few of the international commentators seemed to grasp this detail. It was a far better story if gullible Icelanders had been tricked into dubious genetic research participation.

The Icelandic news travelled the world and the (distorted) debate about informed consent subsequently helped frame debates about biobanks in most other western countries. In the UK, Welcome Trust and the Medical Research Council commissioned work to delineate the ethical problems concerning biobanks (Martin and Kaye, 2000; Spallone and Wilkie, 2000) and investigate public attitudes before the establishment of a new national database (Cragg Ross Dawson, 2000). In this work criticism of presumed consent in Iceland was highlighted. Shortly after, a large-scale project called UK Biobank was initiated with the stated aim of collecting samples and health data from 500,000 individuals. Again the consent issue occupied a central role (Tutton *et al.*, 2004). In public debate, however, the use (and non-use) of stored tissue probably received more intense media coverage in relation to the retention of children's organs at the Alder Hey Hospital and the Bristol Infirmary (Seale *et al.*, 2006). A number of organs had been kept without parental consent and without a clear research protocol or plan of usage. There was no legal demand for consent for retention, but again informed consent helped frame the nature of the problem. Ireland faced a similar media story in relation to the Dunne Inquiry (Cousins *et al.*, 2005). We cannot know what parents truly were concerned about and whether an information sheet and a signature would have provided much comfort, but informed consent was the solution that framed the problem needing to be solved. It provided legislators with a way out of a situation demanding action.

It is impossible here to cover the many different trajectories through which informed consent became the solution to the anxiety that tissue storage began to provoke in policy-making circles in Europe and North America. Nevertheless, for the sake of indicating differences it is worth remarking that in Norway and Sweden – both renowned for their epidemiological research, vast tissue collections and high-quality

registries – the Icelandic experience inspired two interrelated types of activity. On the one hand, some actors wanted to commercialize the existing biobank resources (why should Iceland get all the influx of private investments when population-based registries and biobanks of more or less the same dimensions were already established in these countries?). On the other hand, media and politicians began to question the legitimacy of the existing research infrastructures. Both countries passed specific biobank laws, which made informed consent into a standard requirement for tissue storage. In the context of these welfare states, the moral breach to be avoided was illegitimate state intrusion into the private sphere and, again, the solution was an autonomous choice sealed with a signature (Brekke and Sirnes, 2006; Hoeyer, 2003). In France, a series of scandals concerning therapeutic biobanks received more public attention than research biobanking (Patel, 1993), even if national pride made American use of a French research biobank into a contested issue in academic circles (Rabinow, 1999). But despite the heterogeneity of the problems debated, informed consent once more became a key element of the "solutions" considered when contemplating the "biobank problem" and the consent requirement was entrenched in law already in 1994 (Godard *et al.*, 2003). The plethora of new laws and circulars, nationally and internationally, has caused considerable confusion and has given rise to a call for harmonization of the consent requirement (Bauer *et al.*, 2004; Clayton, 2005 ; Kapp, 2006; Morente and Alonso, 2005). But as pointed out by Maschke and Murrey, it is rarely debated who should be invited to do the harmonization, whether harmonization is indeed feasible, and in whose interest such harmonization would be (Maschke and Murray, 2004).

deCODE conceptualised biobanking as a viable research strategy for a broader group of researchers and made commercialization of tissue-based research appear not only possible, but also desirable. Since the late 1990s, many existing biobanks have considered or even tested options for attracting private investments, and most of the new large-scale biobanks or extensions of existing biobanks involve some element of commercial interaction. However, commercialization has also been part of triggering the sense of anxiety. When biobanks act as profit generating devices, the legitimacy of the research as a pursuit of health is potentially challenged and the motivation of donors endangered. Commercialization raises issues of fairness and benefit sharing (Andrews, 2007; Andrews and Nelkin, 1998; Dickenson, 2005). In addition, commercial exchanges of tissue challenge basic cultural (and legal) distinctions between personhood and commodities (Ertman and Williams, (eds.) 2005; Holland, 2001): what is being exchanged, a thing or a part of person? According to basic legal distinctions it cannot be both (Fox, 2000). Therefore, the increasing involvement of commercial interests contributes to the sense of ethical anxiety. For a commercial endeavour to be successful property rights need to be established, which is difficult when donors do not "own" their bodies and cannot sell them in whole or in parts (Gold, 1996; Grubb, 1998; Laurie, 2002). It was considered whether tissue could be viewed as waste and if waste would constitute abandoned property (McHale, 2000; Parry, 2005). But still, how should commercial rights to tissue collected for prospective biobanks be established (where waste is definitely an inadequate terminology)? How could tissue pass from the state of forming part of a person to become a thing with the attributes associated with commodities?

Intriguingly, again, the solutions suggested have tended to focus on providing the individual with the right to informed consent (rather than with the distribution

of commercial entitlements as such). Not only is informed consent an easier topic to deal with than commercial entitlements, the consent requirement has also helped to circumvent the legal predicament of dealing in something which cannot be sold. Informed consent has come to serve the double function of presenting participation as voluntary *and* of clarifying the ethical status of tissue in between personhood and thing. If *gifting* of tissue can be interpreted as a legal transfer of property rights, informed consent becomes the non-commercial mechanism through which tissue becomes the *property* of a biobank (Landecker, 1999; Tutton, 2004). For some this is expected to preserve human dignity (Perley, 1992). Through the consent procedure the ambiguous entitlements relating to the tissue are sorted out and its status declared: prior to the consent it belongs to the realm of personhood; afterwards to the realm of research with its accompanying commercial entitlements (Hoeyer, 2007).

The influx of money to this research field has been considerable and might even change the outlook of medical research as we know it. Due to the need for shared research infrastructures experimental physicists have long collaborated much more than geneticists. The increasing number of large-scale biobanks could be indicative of similar developments in medicine. In addition to the ones already mentioned, large-scale tissue infrastructures are currently under transformation, under construction or in the planning phase in, e.g., Austria (GATiB), Estonia (Estonian Genome Project), Italy (SharDNA), Japan (Biobank Japan), Quebec (CARTaGENE), Sweden (LifeGene and Medical Biobank/UmanGenomics), Taiwan (Taiwan Biobank), and USA (GRAD, GAIN, GEI), see also (The Secretary's Advisory Committee on Genetics, 2007).[5] Some, such as one in the Kingdom of Tonga, were planned but have already been abandoned, while others have failed commercially (UmanGenomics) but continue as a public research infrastructure (Medical Biobank). For the many new research biobanks, deCODE not only showed the way in terms of a commercial research strategy, but the debate about its (misunderstood) policy on the consent issue also defined the main problem to be debated in relation to commercial genetic research on human tissue: informed consent. In what follows below, debates about the consent requirement are described as they are unfolded in the literature.

Informed consent as an organizationally useful battleground

As indicated above, academic debate cannot be separated from policymaking in relation to the biobank issue. The actors publishing their stance in academic journals tend also to have been engaged in laying out the research infrastructures and legal frameworks described above. However, as we now turn to the published literature we can go into more detail with the long and diverse list of articulated concerns about commercial genetic research on human tissue. Just as the organizational framing described above, academic debates never cease to revolve around informed consent. Informed consent has become the obligatory passage point for academic debate about biobanks. In a sense, the consent requirement provided the "solution" that helped define which problem to discuss. Translating the informed consent requirement from the context of the clinic to tissue based research turned out to be anything but simple.

[5] Find (partial) overviews in (Austin, Harding & McElroy, 2003; Cambon-Thomsen, 2004; Lewis, 2004; Hirtzlin *et al*., 2003).

There was much to discuss – and to criticize. Several researchers foresaw that the consent requirement "would bring research to a standstill" (Marshall, 1998: 2165, see also Furness, 2003; Furness and Sullivan, 2004), and the pros and cons of consent as well as the "how to do it" delivered material for several hundred articles.

The debate has revolved around the amount of *information*, in number of pages, that donors should be given; *when* it should be provided – when samples were taken or when used for research; *how* information should be provided – written or orally; to *whom* – if the donor has died or is incapacitated who should consent; and *what* the information should include – the disease studied, the methods, the funding, the location or the research proposed, etc. The possible complications concomitant with the introduction of informed consent have also received considerable attention: e.g., *wastage* – research projects that must be cancelled; *psychological harm* – how will people under psychological stress feel about being asked to donate?; and *practical problems* – how to contact donors years after the donation (Arnason, 2004; Beskow *et al.*, 2001; Dillner, 2001; Eriksson, 2005; Furness and Sullivan, 2004; Lipworth *et al.*, 2006; McQueen, 1998; Örn, 2003; Regidor, 2004; Cambon-Thomsen *et al.*, 2007; Diest and Savulescu, 2002; Eriksson, 2005; Flemming, 2007). Ironically, a considerable amount of the literature discusses whether informed consent is really an appropriate term at all. Would broad consent be better (since donors cannot be informed about all future research) (Hansson *et al.*, 2006) or perhaps open consent (Nõmper, 2005)? Or an authorization (to use the material) (Arnason, 2004)? Or community consent or group consent (if genetic material is shared, should it be groups or families consenting?) (Greely, 2001; Weldon, 2004; Whong-Barr, 2004)?

Furthermore, the reason for emphasising informed consent differs in the literature (Häyry and Takala, 2007b; Wendler, 2002). It is mostly assumed that everybody agrees about the purpose of informed consent, but this is not so. Some claim that the requirement serves to *protect* the donor, while others claim that it serves to enhance the donor's *autonomy*. Autonomy in turn is understood in numerous ways: to some it relates to dignity and the obligation to act out of duty (O'Neill, 2002); for others it relates to self-determinism and the right to act according to personal preference (Artizzu, 2007). Independently of the function consent is supposed to fulfil, the consent requirement in one form or another has nevertheless come to mediate the relationship between the people from whom the biological material derives and the researchers wanting to access it. How these people are named depends on the understanding of this relationship. Hence, a whole debate has evolved around appropriate terms: does 'donor' imply giving up all rights; is 'participant' a better term or does it transfer too much responsibility; is 'source' a neutral term or is it dehumanizing; and how about 'contributor' to acknowledge the work performed through the act of donation (Sade, 2002; Tutton, 2007; Wendler, 2002)?

Furthermore, the nature of the "problem" that the consent requirement is expected to solve is perceived very differently in various articles. To illustrate the complexity, the various interrelated dimensions of the "biobank problem" figuring in the literature are listed here. They include: *respect* – either for dignity, self-determinism, or contributorship (Wendler, 2002); *privacy* – either in an existential sense or as a practical problem of confidentiality (Nordal, 2007); *risks* – are they serious or minor? (Maschke, 2006); *return of research results to donors* – who would like to know what? Can uncertain results be provided? What about the right not to know? What if

there is no disease treatment? (Renegar *et al.*, 2006); *property rights* – can tissue be an object of ownership and does informed consent help to define this? (Charo, 2004); *commodification* – does commercialization of biobanks infringe human dignity? Does it constitute exploitation? (Rose, 2001); *benefit sharing* – should donors have a share of potential profits? How will public health goals be addressed in a commercial research infrastructure? (Simm, 2005); *dangers of genetic research* in general – will this type of research lead to eugenics? Do we want new types of risk knowledge? Are we tampering with Nature or playing God? (Chadwick, 2001; Rose, 2001); *trust* – is it a value in itself or a means for other values? (Ashcroft, 2000; Helminski, 1994; Sutrop, 2007); and finally, issues of *governance* – what models can accommodate the concerns listed above? What is the role of Institutional Review Boards/Research Ethics Committees and can the system be rethought to better facilitate biobank research? (Gottweis and Zatloukal, 2007; Caulfield and Outerbridge, 2002).

It is interesting how the consent requirement, irrespective of the multiple dimensions and complex set of concerns just listed, has managed to become part of the solution. This might be related to the fact that there are no easy solutions to the complex and occasionally diffuse concerns about commercial genetic biobank research; getting a signature is, at least, not insurmountable. It might seem like an unnecessary obstacle for some pathologists unaccustomed to it, but the alternative would be to rethink research infrastructures more thoroughly. It is not strange if the old saying attributed Mark Twain springs to mind when contemplating this process: if the only tool you got is a hammer, the whole world starts looking like nails. From an organizational perspective the academic debate has provided a wonderfully manageable problem: make sure somebody has signed a piece of paper. But how does this solution relate to donors' concerns? What do we know about donors' views of their interests?

Donor perspectives

A number of surveys have been conducted to uncover the attitudes among donors to the use of human biological material for research providing a very heterogeneous picture.[6] In as far as surveys seek to measure public attitudes to help shape legitimate policies, the resulting measurements contain extraordinarily contradictory conclusions with few messages other than "people feel differently about these issues". Though there are no clear trends, it is possible to infer a few general insights for cautious contemplation.

1) The type of tissue asked for and the position of the donors in relation to the research project seem to influence the view of research on tissue. Cancer patients are generally very supportive of research on their tissue (Malone *et al.*, 2002; Pentz *et al.*, 1999); potential participants in cohort studies are less willing but

[6] Conceivably, the heterogeneity reflects the fact that surveys explore different types of tissue (e.g. tumour/blood/cadavaric material); different types of donors (potential donors/re-contacted donors, and different nationalities/social groups); different affiliation of researchers (biobank internal/external, and different disciplinary affiliation); in relation to different types of biobanks (cohort studies/case-control studies/biotechnological experiments); using different methodological approaches and asking different questions.

still relatively supportive (Cousins *et al.*, 2005; Kettis-Lindblad *et al.*, 2005; Kettis-Lindblad *et al.*, 2007); while the kin of potential cadaveric donors are least likely to accept donation (Womack and Jack, 2003; Womack *et al.*, 2006). The more people feel they need medical research results; the more likely they seem to be to accept donations.

2) Only a minority would never participate in biobank research (Chen *et al.*, 2005; Goodson and Vernon, 2004) but the social groups most likely to abstain differ between national contexts; for example, in the US ethnic minorities and people with poor education will typically abstain (Pentz *et al.*, 2006; Wendler and Emanuel, 2002), while in Sweden it seems to be younger men with higher education who are least likely to participate (Hoeyer *et al.*, 2004; Kettis-Lindblad *et al.*, 2007, see however Nilstun and Hermerén, 2006).

3) A majority, or at least a substantial minority, think the donor should have a say concerning retention of tissue (e.g., Nilstun and Hermerén, 2006; Stegmayr and Asplund, 2002; Wendler and Emanuel, 2002). This is generally interpreted as support of a consent requirement (Merz, 1997), but whether people prefer broad (Chen *et al.*, 2005) or specific consent (Eriksson, 2007; Human Genetics Commission, 2000), and when and under which conditions differs remarkably between the surveys.

4) Commercial access to public biobanks is accepted by a majority (Jack and Womack, 2003; Stegmayr and Asplund, 2002); nevertheless, it is viewed more as a necessary evil than as the preferred research infrastructure (e.g., Cragg Ross Dawson, 2000; Gudmundsdóttir and Nordal, 2007). In a British survey, for example, genetic research results were viewed as belonging to the public (Human Genetics Commission, 2000).

5) Mostly donors are interested in getting access to research results, particularly of relevance to their own health, but the conditions differ widely and national discrepancies also seem to be at stake (Cousins *et al.*, 2005; Hoeyer *et al.*, 2004).

However, irrespective of the finding there always seems to be at least one survey contradicting it.

Further, a number of qualitative studies have been conducted, mostly in northern Europe; interestingly, these studies, which focus on the *reasoning* among potential and actual donors, provide a more homogeneous picture than do the survey measurements – despite using open-ended methodology and multiple research approaches in diverse settings. These studies challenge many of the assumptions underlying the normative ethical and legal debate described above. In particular, informed consent does not seem to serve the purpose of protecting donors (Bister *et al.,* 2009). Donors rarely read, recall or use the information with which they are provided (Busby, 2006; Hoeyer, 2003; Ducournau, 2007). This type of problem with informed consent is well-known beyond the biobank issue (Sugarman *et al.*, 1999). Donors have a number of concerns, in particular in relation to research outlook and commercial interests (Busby, 2004; Skolbekken *et al.*, 2005; Levitt and Weldon, 2005). However, they tend to trust the research institutions conducting the research they contribute to, but the trust is in no way unconditional (Haimes and Whong-Barr, 2004; Skolbekken *et al*., 2005).

Finally, they do not find themselves in a position to personally control the issues worrying them and do not find informed consent helpful in reaching this end (Barr, 2006; Hoeyer, 2004).

An early study indicated that donors had varying ideas about potential benefits to accrue from participation, which would imply that the so-called altruistic motivation often assumed in the ethics literature was far from the type of motivation facilitating participation (Tutton, 2002). Depending on the setting and context, donors have different expectations as to the care they expect to be met with; but people who are willing to donate seem always to expect the care they exhibit through donation to be returned in terms of care for their own health where appropriate and feasible. Couples in infertility treatment are concerned that embryo donations for research compromise their own treatment opportunities (Parry, 2006) but they also see donations as a way to reciprocate the care they have been met with (Svendsen, 2007). Other studies have highlighted how people in the European welfare states see participation as a sort of obligation that is part of benefiting from universal healthcare and medical science (Busby, 2004; Busby, 2006; Hoeyer, 2003; Skolbekken *et al.*, 2005; Svendsen, 2007). People are motivated as much by the context in which they are invited to participate as by the information provided – and they expect medical research facilitated by public health services to benefit everybody (*Ibid*.). A study of donor attitudes in the UK found that there is no clear point in time when donors decide to participate in the study (Haimes and Whong-Barr, 2004) as presumed by the binary choice offered in the consent procedure. A French study specifically investigated how donors viewed the consent process. Interestingly, they saw the consent requirement mostly as a protection of the research institution rather than of themselves and many disliked the procedure (Ducournau, 2007). UK-based studies have found that donors have a number of worries relating to confidentiality, which indicates slightly more emphasis on privacy in the UK than in the Scandinavian countries (Levitt and Weldon, 2005; Weldon, 2007). However, donors everywhere seem to worry about and condemn breaches of confidentiality, and still all who have donated must have decided that such breaches are unlikely in that specific instance. Hence, we cannot know if these differences relate to the approaches and interests of investigators or the donating public. In a study among cancer patient donors in the US the recent HIPAA Privacy Rule (that has been enacted to ensure the privacy of patients and ensure their consent prior to use of their medical records, see Gunn *et al.*, 2004) was even criticized by donors for potentially delaying research (Kaphingst *et al.*, 2006).

All in all, potential and actual donors express nuanced reasoning about the pros and cons of various types of research and research regulation. However, they rarely see themselves as enacting this type of regulation through their donation. They expect the authorities to take care of proper regulation (Hoeyer, 2003). While this can be seen as an expression of trust, it is important to notice that most donors have worries and strong opinions about the type of research they wish to contribute to, and continued trust hinges on the ability to meet their expectations. Concerns in all the many studies typically revolve around confidentiality, benefit-sharing, genetics and commercial involvement. Some donors fear that genetic knowledge will be used to generate a kind of society that marginalizes or exterminates minorities; others fear that we will begin to know things that will not benefit us. Still others are mainly worried about the ability of the research agenda to address public health needs. This type of

worry relates also to commercial involvement. When private investments are part of speeding up public research, it is seen as positive; however, many donors fear that private investments imply that only profitable diseases are investigated. A notion of fairness often seems to be involved, where medical research is supposed to be based on medical needs rather than consumer abilities.

Intriguingly, informed consent is of little help for donors when figuring out whether a biobank is governed according to the standards and aims that they have. The main point of normative ethical and legal debate is poorly related to donor concerns, and empirically speaking it seems to have minimal influence on their decision-making.

State of the art in the field of ethics?

The discrepancy between donor concerns and the ethics literature is worrisome, and so is the remarkable fixation on the consent issue. To evaluate briefly the literature it is worthwhile first to comment on the differences between the qualitative and the quantitative studies, and then add a few comments to the literature in general.

It is striking how the qualitative studies differ from the surveys, in particular in relation to how the consent requirement is viewed. This can probably partly be attributed to the way in which surveys conducted without proper qualitative pilot studies tend to get answers that reflect the questions asked rather than the views that respondents hold. To illustrate the problem with survey data in this field, two surveys in Sweden that I have been part of conducting, will briefly be described (Hoeyer *et al.*, 2004; Hoeyer *et al.*, 2005). One was administered to the general public and one to a group of donors. In both the questions were triangulated to test the reliability of findings from an ongoing qualitative study. In the qualitative study donors were found to pay little attention to informed consent but, nevertheless, expect researchers to respect their intentions with their donation. In the population-based survey respondents were invited to say whether they wanted to provide informed consent (62% did); if they would be willing to delegate decisions to a Research Ethics Committee (67% did); and to rate being personally informed about research on their sample in relation to other concerns that had arisen during interviews (4% found being informed the most important). The survey administered to actual donors had similar responses and furthermore asked whether the respondents remembered having donated a sample for research (65% remembered) and if they were satisfied with the information they had been given (6% were not). Again, being personally informed was what concerned respondents the least in relation to biobank governance. Even if a substantial minority were not aware that they had donated, it did not decrease the satisfaction with the information provided or result in a higher rating of being personally informed. Hence, through a triangulation it was possible to show that even if respondents think they have a right to be asked, consent need not be their primary concern.

Just as the qualitative studies, this again indicates that donors expect to have their wishes respected concerning how their tissue is used. They also expect authorities and/or researchers to ensure that proper safeguards are in place and only fair and appropriate goals are pursued with the research they facilitate. This, however, cannot be read out of the numbers, unless they are interpreted in context. Even more clearly does this type of triangulation show that all such surveys must be read with extreme caution. Surveys are not merely uncovering public opinion; they are constructing what

we get to know about public concerns. When the wrong questions are asked, the main concerns of donors risk remaining unexplored. Public opposition can be triggered by a number of issues other than the consent requirement, and research biobanks thus face a number of potential organizational hazards of which we know very little. There is important work ahead.

Bioethics have fared much better in areas other than biobanking – raising the awareness of important dilemmas and challenges in our everyday practices. The literature on biobanking is mostly dull and sometimes inadequate or even erroneous. It is not unusual to see "reviews" that have managed to gather only studies that support the view held by the authors, despite plenty of available studies contradicting their findings. For example, Shickle found that "all" empirical studies of donor attitudes support a strict specific consent requirement (Shickle, 2006), while Wendler found that "all" available studies support the use of broad consent (Wendler, 2006). Wendler did not see any problem in combining studies from different places and time periods, conducted in different groups and using different methods. Other problems also prevail in the literature. It is assumed that genetic research in Iceland was supposed to rely on presumed consent (Greely, 2007; Swede *et al.*, 2007), basic errors concerning names of biobanks or when they were established as well as confusion of laws regulating therapeutic and research biobanks are fairly common etc. (Gassner, 2007; Maschke, 2005; Weir and Olick, 2004). Further, a number of studies manage to present themselves as being the first on topics, despite several others having been published before – as would have been revealed by anything more than a rudimentary *Medline* search. Also, the importance of informed consent is continually explained by attributing it to the Nuremberg Code following the trials after the Second World War (Kristinsson and Árnason, 2007; Swede *et al.*, 2007). However, informed consent was not introduced with the Nuremberg Code (which mentioned only *voluntary* consent); it was already embedded in the law in Germany in August 1931 but, unfortunately, it did little to protect the Jews, homosexuals and others in the concentration camps. Furthermore, the Nuremberg Code had little if any impact on medical research outside Germany (Annas, 1992; Glantz, 1992). Why then is this type of reference made again and again in the biobank debate? One possible explanation is that it serves a political function of bolstering the necessity of considering informed consent. Of course, nobody would like to compare him- or herself with Dr Mengele. The reference to Nuremberg serves a mythical function. It is part of explaining the gravity of informed consent and the historical accuracy is downplayed to reach the current organizational aim of restructuring human tissue collecting practices with a strengthened consent requirement.

Discussion

The naming and framing of biobanks as ethical problems has taken a peculiar road. Biobanks moved in a few years from forming part of dull routines to feature as widely debated and well-funded research infrastructures. In the process, an almost endless number of concerns have been uttered relating to, for example, commercial genetic research, issues relating to commodification of human tissue, benefit-sharing, risk society, eugenics, fairness, autonomy, dignity, and trust. All these problems seem, however, to have been interpreted through a particular "solution": informed consent.

Irrespective of the nature of the problem they identify, commentators have pointed to the need to ensure that potential donors or their relatives are properly informed and granted a choice. The ability of informed consent to address the concerns uttered is rarely questioned. Even highly sophisticated analyses of deCODE Genetics that focus on the organizational shortcomings with respect to accommodation of a public health agenda, which simultaneously show that Icelanders are very well informed, fail to go beyond informed consent when looking for solutions to the predicament (Merz *et al.*, 2004; Potts, 2002). In fact, informed consent seems to have served the managerially helpful role of limiting the problems biobanks are expected to address in their policies. Thereby the problems are reduced to what is, after all, a manageable task – to get a signature from somebody. In terms of ethical reasoning, the debate has been highly inadequate, but expecting it to be about ethics alone would be missing the point.

A great part of the biobank literature should probably be read as a story about organizational decision-making rather than ethical reasoning. Rather than being guided by academic curiosity, writers have been engaged in finding solutions to a diffuse anxiety relating to genetics, patient rights and commercialisation. Nevertheless, many interesting studies with implications way beyond biobanking have also come about in the process - it has also been fruitful to study the social and ethical implications of biobanking. In particular, the social sciences have contributed a number of insights concerning the dynamics of trust, national and group identity, kinship, failures of benefit-sharing in science, and ethics as policymaking (Busby, 2007; Corrigan and Williams-Jones, 2006; Haddow *et al.*, 2005; Pálsson and Rabinow, 2005; Pálsson, 2007; Petersen, 2005; Prainsack, 2007; Rabinow, 1999; Rose and Novas, 2005; Salter and Jones, 2005). Sadly, there has been limited interaction between the social science literature and the majority of the literature about biobanks, which is published in biological, medical and ethics journals. A distinguished professor of anthropology thus recently managed to claim that debates had moved beyond the consent requirement – in a year that saw more articles on the issue than ever before (Pálsson, 2007). The many interesting insights delivered by social scientists as well as some ethicists and pathologists have had little impact on the legal and organizational debate. Why? Well, if the biobank debate is seen as an organizational event, it is no surprise. When the need for solutions is bigger than the urge for insight into problems, informed consent is relatively easy to translate into action. The debate has delivered a way to move forward in the realization of immense political, financial and scientific interests.

Nevertheless, for ethical as well as organizational reasons, it makes good sense to reconsider the "biobank problem". The empirical studies of donor attitudes point to a number of concerns that are not addressed when focusing all attention on informed consent (Petersen, 2005). If donors really are seen as contributors worthy of respect (Wendler, 2002), biobanks are ethically obliged to take donor concerns seriously. Also, a mismatch between donor interests and research commitments constitutes an organizational vulnerability. Only one bad media story is needed to trigger opposition and widespread opting out unless a biobank infrastructure is designed to accommodate the type of research that donors are willing to advance. Based on what we know about donor attitudes, it appears that different local settings face different challenges in making their research strategy locally legitimate. In most cases, however, it seems obvious that the primary target of intervention should be the financial and political organization and context of the biobank (Häyry and Takala, 2007a). The question that needs to be addressed is how the interests of the donors can be accommodated

by the basic organization of the research. What matters to many people is whether the research addresses health needs rather than markets' size. Therefore funding policies, policies for Intellectual Property Rights (IPR) and licensing schemes, as well as policies for organizational oversight and priority setting, must take a much more prominent role in biobank ethics. Some attempts have been made to design new organizational models for biobanks (Winickoff and Winickoff, 2003; Deschênes and Sallée, 2005), but this work is far from complete. These organizational issues must be complemented with much more concerted engagement with public concerns over genetics and experimental medical research in general. Research is always in danger of losing public legitimacy – it is a consequence of exploring the unknown. The outreach of science today has taken a route that turns public dialogue into a genuine necessity. There are no easy solutions to the complex dilemmas we face – and in the process of establishing clearer policies on priority setting, researchers might come to think through more clearly what types of research they personally find most beneficial. And knowing what you think, and why you have chosen to support one project rather than another, might be the best help you can get when faced with future public criticism and resistance.

Acknowledgments

This work was supported by the Carlsberg Foundation and the Velux Foundation. I would like to thank Richard Tutton and Morten Andreasen for fruitful comments on an earlier draft. All shortcomings and mistakes are my responsibility only.

References

Andrews, L.B. (2007) Harnessing the Benefits of Biobanks. *Journal of Law, Medicine & Ethics* **33**(1), 22-30.

Andrews, L.B., and Nelkin, D. (1998) Whose Body Is It Anyway? Disputes Over Body Tissue in a Biotechnology Age. *The Lancet* **351**, 53-57.

Annas, G.J. (1992) The Nuremberg Code in the United States Courts: Ethics versus Expediency. In *The Nazi Doctors and the Nuremberg Code* eds. G.J. Annas and M.A. Grodin, pp 201-222. Oxford: Oxford University Press.

Árnason, A., and Simpson, B. (2003) Refractions through Culture: The New Genomics in Iceland. *Ethnos* **68**(4), 533-553.

Árnason, G., Nordal, S. and Árnason, V. (Eds.) (2004) *Blood and Data. Ethical, Legal and Social Aspects of Human Genetic Databases*, pp 67-77. Reykjavik: University of Iceland Press.

Arnason, V. (2004). Coding and Consent: Moral Challenges of the Database Project in Iceland. *Bioethics* **18**(1), 27-49.

Artizzu, F. (2007) The informed consent aftermath of the genetic revolution. An Italian example of implementation. *Medicine, Health Care and Philosophy,* (Online first).

Ashcroft, R. (2000) The Ethics of Reusing Archived Tissue for Research. *Neuropathology and Applied Neurobiology* **26**, 408-411.

Austin, M.A., Harding, S., and McElroy, C. (2003) Genebanks: A Comparison of Eight Proposed International Databases. *Community Genetics* **6**(1), 37-45.

Barr, M. (2006) 'I'm not really read up on Genetics': Biobanks and the Social Context of Informed Consent. *BioSocieties* **1,** 251-262.

Bauer, K., Taub, S., and Parsi, K. (2004) Ethical issues in tissue banking for research: a brief review of existing organizational policies. *Theoretical Medicine* **25**, 113-142.

Beskow, L.M., Burke, W., Merz, J.F., Barr, P.A., Terry, S., Penchazadeh, V.B., Gostin, L.O., Gwinn, M., and Khoury, M. (2001) Informed Consent for Population-Based Research Involving Genetics. *Journal of the American Medical Association* **286**(18), 2315-2321.

Bister,M.D., Felt,U., Strassing,M., & Wagner,U. (2009) Refusing the information paradigm: Informed consent, medical research, and patient participation. *Health* (Forthcoming*)*.

Brekke, O.A., and Sirnes, T. (2006) Population Biobanks: The Ethical Gravity of Informed Consent. *BioSocieties* **1**, 385-398.

Busby, H. (2004) Blood Donation for Genetic Research: What Can We Learch from Donors? In *The Gift: The Donation and Exploitation of Human Tissue in Research* eds. R. Tutton and O. Corrigan. London: Routledge.

Busby, H. (2006) Consent, trust and ethics: reflections on the findings of an interview based study with people donating blood for genetic research for research within NHS. *Clinical Ethics* **1**, 211-215.

Busby, H. (2007) Biobanks, bioethics and concepts of donated blood in the UK. In *The View From Here. Bioethics and the Social Sciences* eds. R. de Vries, L. Turner, K. Orfali and C.L. Bosk, pp 179-193. Oxford: Blackwell Publishing.

Cambon-Thomsen, A. (2004) The social and ethical issues of post-genomic human biobanks. *Nature Review Genetics* **5**, 6-13.

Cambon-Thomsen, A., Rial-Sebbag, E., and Knoppers, B.M. (2007) Trends in ethical and legal frameworks for the use of human biobanks. *European Respiratory Journal* **30**, 373-382.

Caulfield, T., and Outerbridge, T. (2002) DNA Databanks, Public Opinion and the Law. *Clinical and Investigative Medicine* **25**(6), 252-256.

Chadwick, R. (2001) Informed Consent and Genetic Research. In *Informed Consent in Medical Research* eds. L. Doyal and J. Tobias, pp 203-210. London: BMJ Books.

Charo, R.A. (2004) Legal Characterizations of Human Tissue. In *Transplanting Human Tissue: Ethics, Policy and Practice* eds. S.J. Youngner, M.W. Anderson and R. Schapiro, pp 101-119. Oxford: Oxford University Press.

Chen, D.T. et al. (2005) Research With Stored Biological Samples: What Do Research Participants Want? *Arch Intern Med* **165**, 652-655.

Clarke, A.E. (1995) Research Materials and Reproductive Science in the United States, 1910-1940. In *Ecologies of Knowledge* ed. S.L. Star, pp 183-225. Albany: State University of New York.

Clayton, E.W. (2005) Informed Consent and Biobanks. *Journal of Law, Medicine & Ethics* **33**(1), 15-21.

Corrigan, O.P. and Williams-Jones, B. (2006) Pharmacogenetics: the bioethical problem of DNA investment banking. *Studies in History and Philosophy of Biological and Biomedical Sciences* **37**, 550-565.

Cousins, G., McGee, H., Ring, L., Conroy, R., Kay, E., Croke, D. and Tomkin, D. (2005) *Public Perceptions of Biomedical Research. A survey of the general population in*

Ireland. Dublin: Health Research Board.

Dabrock, P., Ried, J. and Taupitz, J. (Eds.) (forthcoming) *Trust in Biobanking. Social, Ethical and Legal Aspects of Biobanking*. Heidelberg & Berkeley: Springer Verlag.

Dawson, C.R. (2000) *Public Perceptions of the Collection of Human Biological Samples*. London: The Wellcome Trust and Medical Research Council.

Deschênes, M. and Sallée, C. (2005) Accountability in Population Biobanking: Comparative Approaches. *Journal of Law, Medicine & Ethics* **33**, 41-53.

Dickenson, D. (2005) Human Tissue and Global Ethics. *Genomics, Society and Policy* **1**(1), 41-53.

Diest, P.v. and Savulescu, J. (2002) For and Against: No Consent Should Be Needed for Using Leftover Body Material for Scientific Purposes. *British Medical Journal* **325**, 648-651.

Dillner, J. (2001) Hur Får Biologisk Material Användas? Ny Lagstiftning i Finland. *Läkertidningen* **98**(41), 4478-4479.

Ducournau, P. (2007) The viewpoint of DNA donors on the consent procedure. *New Genetics and Society* **26**(1), 105-116.

Eriksson, K.E. (2007) Sweden. In *The Ethics and Governance of Genetic Databases. European Perspectives* eds. M. Häyry, R. Chadwick, V. Árnason and G. Árnason, pp. 59-65. Cambridge: Cambridge University Press.

Eriksson, S. (2005) Potential Harms, Anonymization, and the Right to Withdraw Consent to Biobank Research. *European Journal of Human Genetics* 13, 1071-1076.

Ertman, M.M. and Williams, J.C. (eds.) (2005) *Rethinking Commodification. Cases and Readings in Law and Culture*. New York: New York University Press.

Flemming, J. (2007) The governance of human genetic research databases in mental health research. *International Journal of Law and Psychiatry* **30**, 182-190.

Fox, M. (2000) Pre-persons, commodities or cyborgs: the legal construction and representation of the embryo. *Health Care Analysis* **8**, 171-188.

Furness, P. (2003) Consent to Using Human Tissue. *British Medical Journal* **329**, 759-760.

Furness, P. and Sullivan, R. (2004) The Human Tissue Bill. Criminal Sanctions Linked to Opaque Legislation Threaten Research. *British Medical Journal* **328**, 533-534.

Gassner, U.M. (2007) Legal Aspects of Tissue Banking. *Pathobiology* **74**, 270-274.

Gibbons, S.M. (2007) Are UK genetic databases governed adequately? A comparative legal analysis. *Legal Studies* **27**, 312-342.

Glantz, L.H. (1992) The influence of the Nuremberg Code on U.S. Statutes and Regulations. In *The Nazi Doctors and the Nuremberg Code* eds. G.J. Annas and M.A. Grodin, pp 183-200. Oxford: Oxford University Press.

Godard, B., Schmidtke, J., Cassiman, J.-J. and Aymé, A. (2003) Data storage and DNA banking for biomedical research: informed consent, confidentiality, quality issues, ownership, return of benefits. A professional perspective. *European Journal of Human Genetics* **11**, 88-122.

Gold, E.R. (1996) *Body parts. Property rights and the ownership of human biological materials.* Washington DC: Georgetwon University Press.

Goodson, M.L. and Vernon, B.G. (2004) A Study of Public Opinion on the Use of Tissue Samples from Living Subjects for Clinical Research. *Journal of Clinical Pathology* **57**, 135-138.

Gottweis, H. and Zatloukal, K. (2007) Biobank Governance: Trends and Perspectives. *Pathobiology* **74**, 206-211.

Greely, H. (2001) Informed Consent and Other Ethical Issues in Human Population Genetics. *Annual Review of Genetics* **35**, 785-800.

Greely, H.T. (2007) The Uneasy Ethical and Legal Underpinnings of Large-Scale Genomic Biobanks. *Annual Reviews of Genomics and Human Genetics* **8**, 343-364.

Grubb, A. (1998) 'I, Me, Mine': Bodies, Parts and Property. *Medical Law International* **3**, 299-317.

Gudmundsdóttir, M.L. and Nordal, S. (2007) Iceland. In *The Ethics and Governance of Human Genetic Databases* eds. M. Häyry, R. Chadwick, V. Árnason and G. Árnason, pp 53-57. Cambridge: Cambridge University Press.

Gunn, P.P., Fremont, A.M., Botrell, M., Shugarman, L.R., Galegher, J. and Bikson, T. (2004) The Health Insurance Portability and Accountability Act Privacy Rule - A Practical Guide for Researchers. *Medical Care* **42**(4), 321-327.

Haddow, G., Laurie, G., Cunningham-Burley, S., & Hunter, K. (2007) Benefit-Sharing: Public Solutions to Private Interests? *Social Science & Medicine* **64**, 272-282.

Haimes, E. and Whong-Barr, M. (2004) Competing Perspectives on Reasons for Participation and Non-Participation in the North Cumbria Community Genetics Project. In *Genetic Databases: Socio-ethical Issues in the Collection and Use of DNA* eds. R. Tutton and O. Corrigan. London: Routledge.

Hansson, M.G., Dillner, J., Bartram, C.R., Carlson, J.A. and Helgesson, G. (2006). Should Doners be Allowed to Give Broad Consent to Future Biobank Research? *The Lancet Oncology* **7**, 266-269.

Häyry, M., R. Chadwick, V. Árnason and G. Árnason (Eds.) (2007) *The Ethics and Governance of Human Genetic Databases*. Cambridge: Cambridge University Press.

Häyry, M. and Takala, T. (2007a) Bioethical analysis of the results: how well do laws and regulations address people's concerns? In *The Ethics and Governance of Human Genetic Databases* eds. M. Häyry, R. Chadwick, V. Árnason and G. Árnason, pp 249-256. Cambridge: Cambridge University Press.

Häyry, M. and Takala, T. (2007b) American principles, European values and the mezzanine rules of ethical genetic databanking. In *The Ethics and Governance of Human Genetic Databases* eds. M. Häyry, R. Chadwick, V. Árnason and G. Árnason, pp 14-36. Cambridge: Cambridge University Press.

Helgason, H.H. (2007) Consent and population genetic databases: a comparative analysis of the law in Iceland, Sweden, Estonia and the UK. In *The Ethics and Governance of Human Genetic Databases* eds. M. Häyry, R. Chadwick, V. Árnason and G. Árnason, pp 97-107. Cambridge: Cambridge University Press.

Helminski, F. (1994) Formalities, Good Faith, and Tissues Donation. *Mayo Clin Proc* **69**, 985-986.

Hirtzlin, I., Dubreuil, C., Préaubert, N., Duchier, J., Jansen, B., Simon, J., Lobato de Faria, P., Perez-Lezaun, A., Visser, B., Williams, G.D. and Cambon-Thomsen, A. (2003) An Emperical Survey on Biobanking of Human Genetic Material and Data in six EU Countries. *European Journal of Human Genetics* **11**, 475-488.

Hodgson, J. (1998) A Genetic Heritage Betrayed or Empowered? *Nature Biotechnology* **16**, 1017-1021.

Hoeyer, K. (2003) "Science is Really Needed - That's All I Know". Informed Consent and the Non-Verbal Practices of Collecting Blood for Genetic Research in Sweden. *New Genetics and Society* **22**(3), 229-244.

Hoeyer, K. (2004) Ambiguous Gifts. Public Anxiety, Informed Consent and Commercial Genetic Biobank Research. In *Genetic Databases: Socio-ethical Issues in the Collection and Use of DNA* eds. R. Tutton and O. Corrigan, pp 97-116. London: Routledge.

Hoeyer, K. (2007) Person, Patent and Property: A Critique of the Commodification Hypothesis. *BioSocieties* **2**(3), 327-348.

Hoeyer, K., Olofsson, B.-O., Mörndal, T. and Lynöe, N. (2004) Informed Consent and Biobanks: A Population-Based Study of Attitudes Towards Tissue Donation for Genetic Research. *Scandinavian Journal of Public Health* **32**, 224-229.

Hoeyer, K., Olofsson, B.-O., Mörndal, T. and Lynöe, N. (2005) The Ethics of Research Using Biobanks: Reason to Question the Importance Attributed Informed Consent. *Archives of Internal Medicine* **165**, 97-100.

Holland, S. (2001) Contested Commodities at Both Ends of Life: Buying and Selling Gametes, Embryos, and Body Tissues. *Kennedy Institute of Ethics Journal* **11**(3), 263-284.

Human Genetics Commission (2000) *Public attitudes to human genetic information. People's Panel Quantitative Study conducted for the Human Genetics Commission*. London: Human Genetics Commission.

Jack, A. and Womack, C. (2003) Why surgical patients do not donate tissue for commercial research: review of records. *British Medical Journal* **327**, 262.

Jeffers, B.R. (2001) Human Biological Materials in Research: Ethical issues and the Role of Stewardship in Minimizing Research Risks. *Advances in Nursing Science* **24**(2), 32-46.

Jenkins, G.L. and Sugarman, J. (2005) The importance of cultural consideration in the promotion of ethical research with human biologic material. *Journal of Laboratory and Clinical Medicine* **145**(3), 118-124.

Kapp, M.B. (2006) Ethical and legal issues in research involving human subjects: do you want a piece of me? *Journal of Clinical Pathology* **59**, 335-339.

Kaye, J. (2007) Regulating human genetic databases in Europe. In *The Ethics and Governance of Human Genetic Databases* eds. M. Häyry, R. Chadwick, V. Árnason and G. Árnason, pp 91-95. Cambridge: Cambridge University Press.

Keller, E.F. (2000) *The Century of the Gene.* Cambridge, Massachusetts: Harvard University Press.

Kettis-Lindblad, Å., Ring, L., Viberth, E. and Hansson, M.G. (2005) Genetic Research and Donation of Tissue Samples to Biobanks. What do Potential Sample Donors in the Swedish General Public Think? *The European Journal of Public Health* (Supplement).

Kettis-Lindblad, Å., Ring, L., Viberth, E. and Hansson, M.G. (2007). Perceptions of potential donors in the Swedish public towards information and consent procedures in relation to use of human tissue samples in biobanks: A population-based study. *Scandinavian Journal of Public Health* **35**, 148-156.

Kjellberg, L., Wang, Z., Wiklund, F., Edlund, K., Angstrom, T., Lenner, P., Sjoberg, I., Hallmans, G., Wallin, K.L., Sapp, M., Schiller, J., Wadell, G., Mahlck, C.G. and Dillner, J. (1999) Sexual behaviour and papillomavirus exposure in cervical

intraepithelial neoplasia: a population-based case-control study. *Journal of General Virology* **80**(2), 391-398.

Knoppers, B. and Laberge, C. (1995) Research and Stored Tissue. Persons as Sources, Samples as Persons? *Journal of the American Medical Association* **274**(22), 1806-1807.

Knoppers, B.M. (1999) Status, Sale and Patenting of Human Genetic Material: An International Survey. *Nature Genetics* **22**, 23-26.

Koch, L. (2004) The Meaning of Eugenics: Reflections on the Government of Genetic Knowledge in the Past and the Present. *Science in Context* **17**(3), 315-331.

Korts, K., Weldon, S. and Gudmundsdóttir, M.L. (2004) Genetic databases and public attitudes: A comparison of Iceland, Estonia and the UK. *Trames* **8**(58/53) (1/2), 131-149.

Kristinsson, S. and Árnason, V. (2007) Informed consent and human genetic database research. In *The Ethics and Governance of Human Genetic Databases* eds M. Häyry, R. Chadwick, V. Árnason and G. Árnason, pp 199-216. Cambridge: Cambridge University Press.

Landecker, H. (1999) Between Beneficence and Chattel: The Human Biological in Law and Science. *Science in Context* **12**(1), 203-225.

Laurie, G. (2002) Privacy *and* Property. *Genetic Privacy. A Challenge to Medico-Legal Norms*, pp 299-328. Cambridge: Cambridge University Press.

Levitt, M. and Weldon, S. (2005) A Well Placed Trust?: Public Perceptions of the Governance of DNA Databases. *Critical Public Health* **15**(4), 311-321.

Lewis, G. (2004) Tissue Collection and the Pharmaceutical Industry: investigating corporate biobanks. In *Genetic Databases. Socio-ethical issues in the collection and use of DNA* eds R. Tutton and O. Corrigan, pp 181-202. London: Routledge.

Lindblom, C.E. (1959) The Science of "Muddling Through". *Public Administration Review* (19), 79-88.

Lindee, S., Goodman, A. and Heath, D. (2003) Anthropology in the Age of Genetics. Practice, Discourse, and Critique. In *Genetic Nature/Culture. Anthropology and Science Beyond the Two-Culture Divide* eds. A. Goodman, D. Heath and S. Lindee, pp 1-19. Berkeley: University of California Press.

Lipworth, W., Ankeny, R. and Kerridge, I. (2006) Consent in crisis: the need to reconceptualize consent to tissue banking research. *Internal Medicine Journal* **36**, 124-128.

Mackenzie, A. (2003) Bringing Sequences to Life: How Bioinformatics Corporealizes Sequence Data. *New Genetics and Society* **22**(3), 315-332.

Malone, T., Catalano, P.J., O'Dwyer, P.J. and Giantonio, B. (2002) High Rate of Consent to Bank Biologic Samples for Future Research: The Eastern Cooperative Oncology Group Experience. *Journal of the National Cancer Institute* **94**(10), 769-771.

March, J.G. and Olsen, J.P. (1976) Organizational Choice under Ambiguity. In *Ambiguity and Choice in Organizations* eds. J.G. March and J.P. Olsen, pp 10-23. Oslo: Universitetsforlaget.

Marshall, E. (1998) Panel Proposes Tighter Rules for Tissue Studies. *Science* **282**(5397), 2165-2166.

Martin, P. and Kaye, J. (2000) The Use of Large Biological Sample Collections in Genetics Research: Issues for Public Policy. *New Genetics and Society* **19**(2), 165-191.

Maschke, K.J. (2005) Navigating an ethical patchwork - human gene banks. *Nature Biotechnology* **23(**5), 539-545.

Maschke, K.J. (2006) Alternative Consent Approaches for Biobank Research. *The Lancet Oncology* **7**, 193-194.

Maschke, K.J. and Murray, T.H. (2004) Ethical issues in tissue banking for research: the prospects and pitfalss of setting international standards. *Theoretical Medicine* **25**, 143-155.

McHale, J. (2000) Waste, ownership and bodily products. *Health Care Analysis* **8**, 123-135.

McQueen, M.J. (1998) Ethical and Legal Issues in the Procurement, Storage and Use of DNA. *Clinical Chemistry and Laboratory Medicine* **36**(8), 545-549.

Merz, J.F. (1997) Psychosocial Risks of Storing and Using Human Tissues in Research. *Risk: Health, Safety and Environment* **8**, 235-248.

Merz, J.F., McGee, G.E. and Sankar, P. (2004) "Iceland Inc."?: On the Ethics of Commercial Population Genomics. *Social Science & Medicine* **58**(6), 1201-1209.

Morente, M.M. and Alonso, S. (2005) Current challenges of human tumor banking. *Hematological Oncology* **23**, 54-56.

Morgan,L. (2002). "Properly Disposed of": A History of Embroyo Disposal and the Changing Claims on Fetal Remains. *Medical Anthropology 21*(3), 247-274.

Nilstun, T. and Hermerén, G. (2006) Human tissue samples and ethics - attitudes of the general public in Sweden to biobank research. *Medicine, Health Care and Philosophy* **9**, 81-86.

Nõmper, A. (2005) *Open Consent - A New Form of Informed Consent for Population Genetic Databases*, pp 5-260. Tartu University.

Nordal, S. (2007) Privacy. In *The Ethics and Governance of Human Genetic Databases* eds. M. Häyry, R. Chadwick, V. Árnason and G. Árnason, pp 181-189. Cambridge: Cambridge University Press.

Novas, C. and Rose, N. (2000) Genetic risk and the birth of the somatic individual. *Economy and Society* **29**(4), 485-513.

O'Neill, O. (2002) *Autonomy and Trust in Bioethics*. Cambridge: Cambridge University Press.

Örn, P. (2003) Försenade Rutiner Drabbar Patologer. *Läkertidningen* **100**(5), 300.

Pálsson, G. (2007) *Anthropology and the New Genetics*. New York: Cambridge University Press.

Pálsson, G. and Harðardóttir, K. (2002) For Whom the Cell Tolls. *Current Anthropology* **43**(2), 271-301.

Pálsson, G. and Rabinow, P. (2005) The Iceland Controversy: Reflections on the Trans-National Market of Civic Virtue. In *Global Assemblages. Technology, Politics, and Ethics as Anthropological Problems* eds. A. Ong and S. Collier, pp 91-103. Oxford: Blackwell.

Parry, B. (2005) The New Human Tissue Bill: Categorization and Definitional Issues and their Implications. *Genomics, Society and Policy* **1**(1), 74-85.

Parry, S. (2006) (Re)constructing Embryos in Stem Cell Research: Exploring the Meaning of Embryos for People Involved in Fertility Treatments. *Social Science & Medicine* **62**, 2349-2359.

Patel, T. (1993) France's troubled transplant trade. *New Scientist* **3**(139), 12-13.

Pentz, R.D., Billot, L. and Wendler, D. (2006) Research on Stored Biological Samples:

Views of African American and White American Cancer Patients. *American Journal of Medical Genetics* **140A**, 733-739.

Pentz, R.D. et al. (1999) Informed Consent for Tissue Research. *Journal of the American Medical Association* **282**(17), 1625.

Perley, S.N. (1992) From control over one's body to control over one's body parts: extending the doctrine of informed consent. *New York University Law Review* **67**(2), 335-365.

Petersen, A. (ed.) (2005) Biobanks: Challenges for "Ethics". Special issue. *Critical Public health* **15**(4).

Petersen, A. (2005) Securing Our Genetic Health: Engendering Trust in UK Biobank. *Sociology of Health and Illness* **27**(2), 271-292.

Petersen, A. and Gottweis, H. (Eds.) (2008) *Biobanks: Governance in Comparative Perspective* London: Routledge.

Potts, J. (2002) At Least Give the Natives Glass Beads: An Examination of the Bargain Made between Iceland and deCODE Genetics with Implications for Global Bioprospecting. *Virginia Journal of Law and Technology* **7**(8), 1-40.

Prainsack, B. (2007) Research populations: biobanks in Israel. *New Genetics and Society* **26**(1), 85-103.

Rabinow, P. (1996) *Making PCR. A Story of Biotechnology.* Chicago: University of Chicago Press.

Rabinow, P. (1999) *French DNA. Trouble in Purgatory.* Chicago: University of Chicago Press.

Regidor, E. (2004) The Use of Personal Data from Medical Records and Biological Materials: Ethical Perspectives and the Basis for Legal Restrictions in Health Research. *Social Science and Medicine* **59**(9), 1975-1984.

Renegar, G., Webster, C.J., Stuerzbecher, S., Harty, L., Ide, S.E., Balkite, B., Rogalski-Salter, T.A., Cohen, N., Spear, B.B., Barnes, D.M. and Brazell, C. (2006) Returning genetic research results to individuals: points-to-consider. *Bioethics* **20**(1), 24-36.

Rose, H. (2001) *The Commodification of Bioinformation: The Icelandic Health Sector Database.* London: The Wellcome Trust.

Rose, N., and Novas, C. (2005) Biological Citizenship. In *Global Assemblages. Technology, Politics, and Ethics as Anthropological Problems* eds. A. Ong and S.J. Collier, pp 439-463. Oxford: Blackwell Publishing.

Rothman, D.J. (1991) *Strangers at the Bedside. A History of How Law and Bioethics Transformed Medical Decision Making.* New York: BasicBooks.

Sade, R. (2002) Research on Stored Biological Samples Is Still Research. *Archives of Internal Medicine* **162**, 1439-1440.

Salter, B. and Jones, M. (2005). Biobanks and Bioethics: The Politics of Legitimation. *Journal of European Public Policy* **12**(4), 710-732.

Seale, C., Cavers, D. and Dixon-Woods, M. (2006) Commodification of Body Parts: By Medicine or by Media? *Body & Society* **12**(1), 25-42.

Shickle, D. (2006) The consent problem within DNA biobanks. *Studies in History and Philosophy of Biological and Biomedical Sciences* **37**, 503-519.

Simm, K. (2005) Benefit-sharing: An Inquiry Regarding the Meaning and Limits of the Concept in Human Genetic Research. *Genomics, Society and Policy* **1**(2), 29-40.

Skolbekken, J.-A., Ursin, L.Ø., Solberg, B., Christensen, E. and Ytterhus, B. (2005)

Not Worth the Paper it's Written on? Informed Consent and Biobank Research in a Norwegian Context. *Critical Public health* **15**(4), 335-347.

Solbakk, J.H., Holm, S. and Hofmann, B. (Eds.) (2008, *forthcoming*) *The Ethics of Research Biobanking.* London: Springer Verlag

Spallone, P. and Wilkie, T. (2000) The Research Agenda in Pharmacogenetics and Biological Sample Collections - A View from the Wellcome Trust. *New Genetics and Society* **19**(2), 193-205.

Stegmayr,B., & Asplund,K. (2002) Informed consent for genetic research on blood stored for more than a decade: a population based study. *British Medical Journal* **325**(7365), 634-635.

Stephenson, J. (1996) Pathologists Enter Debate on Consent for Genetic Research on Stored Tissue. *Journal of the American Medical Association* **275**(7), 503-504.

Sugarman, J., McCrory, D., Powell, D., Krasny, A., Adams, B., Ball, E. and Cassell, C. (1999) Empirical Research on Informed Consent. An Annotated Bibliography. *Hastings Center Report* Special Supplement, 1-42.

Sutrop, M. (Ed.) (2004) Special Issue. *Trames* **8**(1/2).

Sutrop, M. (2007) Trust. In *The Ethics and Governance of Human Genetic Databases* eds. M. Häyry, R. Chadwick, V. Árnason and G. Árnason, pp 190-198. Cambridge: Cambridge University Press.

Svendsen, M.N. (2007) Mellem reproduktiv og regenerativ medicin. Donation som handlerum i fertilitetsklinikken. In *Håbets teknologi. Samfundsvidenskabelige perspektiver på stamcelleforskning i Danmark* eds. L. Koch and K. Høyer, pp 176-200. Copenhagen: Munksgaard.

Swede, H., Stone, C.L. and Norwood, A.R. (2007) National population-based biobanks for genetic research. *Genet Med* **9**(3), 141-149.

Tatarenko, A. (2006) European Regulations and Their Impact on Tissue Banking. *Cell Tissue Banking* **7**, 231-235.

The Secretary's Advisory Committee on Genetics, Health and Society (2007) *Policy Issues Associated with Undertaking a New large U.S. Population Cohort Study of Genes, Environment, and Disease.* Department of Health & Human Services USA.

Tutton, R. (2002) Gift Relationships in Genetics Research. *Science as Culture* **11**(4), 524-542.

Tutton, R. (2004) Person, Property and Gift: Exploring Languages of Tissue Donation to Biomedical Research. In *Genetic Databases: Socio-ethical Issues in the Collection and Use of DNA* eds. R. Tutton and O. Corrigan, London: Routledge.

Tutton, R. (2007) Constructing participation in genetic databases. Citizenship, governance and ambivalence. *Science, Technology and Human Values* **32**(2), 172-195.

Tutton, R. and Corrigan, O. (Eds.) (2004) *Genetic Databases. Socio-ethical issues in the collection and use of DNA*. London: Routledge.

Tutton, R., Kaye, J. and Hoeyer, K. (2004). Governing UK Biobank: The Importance of Ensuring Public Trust. *TRENDS in Biotechnology* **22**(6), 284-285.

Waldby, C. and Mitchell, R. (2006) *Tissue Economies. Blood, Organs, and Cell Lines in Late Capitalism.* London: Duke University Press.

Weir, R. (Ed.) (1998) *Stored Tissue Samples. Ethical, Legal and Public Policy Aspects.* Iowa City: University of Iowa Press.

Weir, R.F. and Olick, R.S. (2004) *The Stored Tissue Issue. Biomedical Research, Ethics, and Law in the Era of Genomic Medicine.* Oxford: Oxford University Press.

Weiss, C.H. (1986) Research and Policy-making: A Limited Partnership. In *The Use and Abuse of Social Science* ed. F. Heller, pp 214-235. London: Sage.

Weldon, S. (2004) 'Public Consent' or 'Scientific Citizenship'? What counts as Public Participation in Population-Based DNA Collections? In *Genetic Databases: Socio-Ethical Issues in the Collection and Use of DNA* eds. R. Tutton and O.Corrigan, pp 161-180. London: Routledge.

Weldon, S. (2007) United Kingdom. In *The Ethics and Governance of Human Genetic Databases* M. Häyry, R. Chadwick, V. Árnason and G.Árnason, pp 66-72. Cambridge: Cambridge University Press.

Wendler, D. (2002) What research with stored samples teaches us about research with human subjects. *Bioethics* **16**(1), 33-54.

Wendler, D. (2006) One time general consent for research on biological samples. *British Medical Journal* **332**, 544-547.

Wendler, D. and Emanuel, E. (2002) The Debate over Research on Stored Biological Samples: What Do Sources Think? *Archives of Internal Medicine* **162**, 1457-1462.

Whong-Barr, M. (2004) Informed Consent and the Shaping of British and US Population-Based Genetic Research. In *Shaping Science & Technology Policy: The Newx Generation of Research* eds. D. Guston and D. Sarawitz. Madison: University of Wisconsin Press.

Winickoff, D.E. and Winickoff, R.N. (2003) The Charitable Trust as a Model for Genomic Biobanks. *New England Journal of Medicin* **349**(12), 1180-1184.

Womack, C. and Jack, A. (2003) Family attitudes to research using samples taken at coroner's postmortem examinations: review of records. *British Medical Journal* **327**, 781-782.

Womack, C., Pope, J., Jack, A. and Semple, C. (2006) Cadaveric Tissue Retrieval Service for Research: One-year Review and Options for the Future. *Cell and Tissue Banking* **7**, 211-214.

Youngner, S.J., Anderson, M.W. and Schapiro, R. (Eds.) (2004) *Transplanting Human Tissue: Ethics, Policy and Practice*. Oxford: Oxford University Press.