4 Research Uses of Biobanks

- Personalised medicine -Pharmacogenomics - (1)match drug to patient for effectiveness (Herceptin), and
(2)Minimise patient adverse drug reactions (ADRs)
(3) *Combinatorial* therapy (eg stem cells and drugs).
- Failure to improve clinical evaluation [of genetic tests] would undermine the development of personalised medicine in the 21st century, and lead to a new generation of medical technology of unclear clinical value. (Melzer et al. *Phg Foundation Research Report* Feb 2008)

5 Technical Challenges of Biobanks

Rand Corporation study -inconsistencies

- Number of data points to be collected for each individual sample
- Coding of the collected sample and protection by encryption codes (Privacy Enhancement Technology –PETs)
- Access only to authorised biobank employees.
- Collection/testing facilities accreditation standards.
- Sample collection and storage must be quality assured and not tainted by human/process error

5 Technical Challenges of Biobanks

- Industry standards for biobanks,
- *First-Generation Guidelines for NCI-Supported BioRepositories (*National Cancer Institute, National Institutes of Health, U.S Health /Human Services)
- *International Society for Biological and Environmental Repositories* (ISBER).

6 Ethical/legal Challenges

1 Privacy and Confidentiality

- Preventing improper access or release
- *Privacy legislation* information be relevant to the purpose for which it is collected *and* access to personal genetic information.

2 Public Consultation and Engagement .

- Public engagement a major feature of the developments eg biobanks (See OECD (2007) particularly Chapter 3.5 *Public Engagement in the Establishment of a Population Database).*
- Public trust and accountability

6 Ethical/legal Challenges

3 Consent: Future biobank projects - re-contacting participants for new information, new uses, or new research.

- (1) *Limited /specific consent* for research for use of sample for a specific project, or
- (2) *Qualified/follow-up* consent where participant wishes to be contacted in future if there is any extension or substantial variation from original research project, or
- (3) *Full/unspecified* consent to use of sample in all future research ("blanket'/"broad" consent is major issue)
- Children (UK not recruiting –Consent at 18?)

6 Ethical/legal Challenges

4 Health Related Information Policy required on whether to reveal health information to participants during research (UK Biobank does not as a policy).

5 Withdrawal from project at different levels,

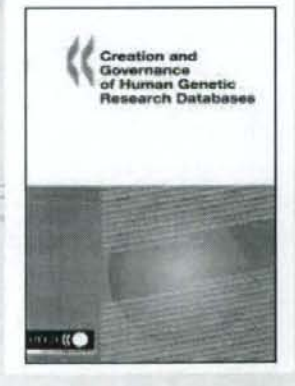
- (!)complete withdrawal and destruction of samples;
- (2)allow use of sample but not participate in any way;
- (3)retention of sample with withdrawal from future projects.

7 Governance

Establishment and Proper Research Governance
-governance structures appropriate for primary research focus and protection of the interests of the research participants.

- UK Biobank, *Ethics and Governance Framework*, Version 2.
- OECD *Creation and Governance of Human Genetic Research Databases* (2007)
- Good governance as a condition of broad consent?

7 Governance



7 Governance

- OECD -*Creation and Governance of Human Genetic Research Databases* (2007)
- Chapter 2. Human Genetic Research Databases
- Chapter 3. Establishment of a HGRD (Public Engagement in the Establishment of a Population Database)
- Chapter 4. Data and Sample Collection and Management
- Chapter 5. Database Management and Governance
- Chapter 6. Commercialisation Considerations
- Chapter 7. Conclusions
- Note *Guidelines* expected in mid 2009 (Draft circulated for comment late 2008)

Conclusions

- OECD Creation and Governance of Human Genetic Research Databases *Guidelines* awaited
- The need for a "chain of responsibility" (German/French Declaration)
- Consent
- Solidarity & Benefit Sharing –Research and health care products?) UNESCO *Universal Declaration on Bioethics and Human Rights* 2005
- Harmonisation

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- *First-Generation Guidelines for NCI-Supported BioRepositories* April 2006, National Cancer Institute, National Institutes of Health, U.S Department of Health and Human Services http://biospecimens.cancer.gov/biorepositories/First%20Generation%20Guidelines%20042006.pdf
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- UK Biobank, *Ethics and Governance Framework*, Version 2.0) Wellcome Trust and Medical Research Council and Department of Health UK, July 2006 http://www.ukbiobank.ac.uk/ethics/egf.php
- German National Ethics Council and the French National Consultative Ethics Committee for Health and Life Sciences, *Joint Declaration*, The European Group on Ethics (EGE) in Science and New Technologies to the European Commission Ethically Speaking Newsletter, Issue 5, August 2005 at 27

International Symposium

Biobank and Genomic Research

- Bioethics of Genomic Medicine -

Ethics, Law and Governance of Biobanks

Donald Chalmers,
University of Tasmania

22nd March, 2009

Kyoto University Clock Tower International Exchange Hall III

Professor Don Chalmers*

Faculty of Law School, University of Tasmania

1 INTRODUCTION

This chapter examines the legal principles and rules for human genetic research with particular emphasis on the development of collections of tissue samples and data held in human genetic research databases. This century has been described by Francis Collins as the Genome Era[1] in science and medicine, acknowledging the volume and intensity of genomic research[2] in both the public and private sectors. Human tissue samples are essential tools for genomic research and "translating biomedical research into real improvements in health care"[3]. The German National Ethics Council[4] has noted the potential of biobanks for the identification of causes of disease and for breakthroughs in medical and pharmaceutical research and the "particularity of biobanks, which…lies in their twofold character, as collections of

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[1] *Australian Biotechnology News* July 4 2003 at p 8.

[2] Knoppers, BM and Chadwick, R "Human Genetic Research: Emerging Trends in Ethics" (2005) 6 *Nature Reviews Genetics* 75-79. See also the special issue of (2007) 18 *King's Law Journal*, 201-311 with articles by Gibbons, SMC, Kaye, J "Governing Genetic Databases: Collection, Storage and Use" at 201-208 ; Caulfield, T "Biobanks and Blanket Consent: The Proper Place of the Public Good and Public Perception Rationales" at 209-226 ;Campbell, AV "The Ethical Challenges of Genetic Databases: Safeguarding Altruism and Trust" at 227-245;Brownsword, R "Genetic Databases: One for All and All for One?"at 247-273; Beyleveld D, "Data Protection and Genetics: Medical Research and the Public Good" at 275-289; Knoppers, BM, et al "Genomic Databases and International Collaboration" at 291-311

[3] Genetic Engineering News Vol 25:No 3 (2005) at 1.

[4] Nationaler Ethikrat , Opinion on Biobanks for Research Berlin 2004 at http://www.ethikrat.org

both samples and data".[5] Pharmacogenetic research into genetic variability in drug response may be substantially advanced by biobanking.[6] Tissue samples, in the form of DNA or RNA samples, cell lines, tissues, cell preparations or plasma/blood samples, are essential tools for pharmacogenomic research and analysis that aims to identify potential biomarkers[7] or drug targets by any of the new generation genomic tests utilising DNA marker, RNA expression level or protein activity. Unsurprisingly, many pharmaceutical companies operate biobank collections for research purposes and to enrol suitable clinical trial recruits so as to minimise side effects and achieve better results. Biobanks are important resources for medical health research that may benefit current patients but are also aimed at long-term research for future benefits[8].

Ethical and social issues[9] surround biobanks, apart from the technical and scientific issues. Human tissue samples held in human genetic research databases will usually be coded, making the samples potentially re-identifiable[10]. This raises the issue of privacy of the genetic information. Patient identification may be required for follow-up of results or result validation. There are doubts whether de-identification is realistic as a link back to the patient may be required, particularly in disease identification studies. Such distinctions are critical in the design, conduct and reporting of human genetic research and pharmacogenomic studies. It has been recognised that complete guarantees of individual privacy are unrealistic in health research. Participant re-contact may also be required by the biobank[11] to collect new information or to seek consent for new approved research uses or a new study.

[5] Ibid at 21

[6] See Shastry,B "Pharmacogenetics and the Concept of Individualized Medicine" (2006) 6 *The Pharmacogenomics Journal* 16-21. The Generation Scotland project, which is run by a consortium of the medical schools in Scotland with Scottish Executive funding, has this as an explicit objective: http://www.generationscotland.org

[7] A bio-marker is a physiological response or a laboratory test that occurs in association with a pathological process that has possible diagnostic and/or prognostic utility.

[8] Kaiser J "Biobanks: Population Databases Boom, from Iceland to the U.S." (2002) 298 *Science* (5596), 1158-1161.

[9] Cambon-Thomsen, A, et al "The social and ethical issues of post-genomic human biobanks" (2004) 5 *Nature Reviews Genetics*, (11) 866-873.

[10] The term is not precise as has been noted by Knoppers, BM and Saginur, M "The Babel of genetic data terminology" (2005) 23 *Nature Biotechnology* 925-927

[11] See UK Biobank, Ethics and Governance Framework, Version 2.0 Wellcome Trust and Medical Research Council and Department of Health UK, July 2006 at 10 http://www.ukbiobank.ac.uk/ethics/egf.php

Linkage may also be required to enable recontact of participants for future research projects, to follow up a participant to pass on clinically significant results or, possibly to recruit for a prospective clinical trial. There has to be an effective balance between individual interests in privacy with the public interest in promoting high quality public health research. Apart from the important legal issue of participant privacy, there is also a mixed range of legal issues[12] dealing with participant consent, research governance, human tissue, material (tissue) transfer agreements, employee confidentiality, commercialization, benefit-sharing and international collaboration.

It is essential that all human research be conducted with integrity and according to the highest ethical standards. This is even more important where large genetic research database collections have been assembled. Public trust[13] is an essential pre-condition for the successful operation and future research benefit of human genetic research databases, sometimes referred to as biobanks.

This chapter considers the regulation required to balance individual interests in privacy with the public interest in effective and reliable research. This issue is particularly salient in relation to genetic research databases where the balance must be made between the proper protections of those recruited as tissue sample providers with the public interest. This chapter does not discuss forensic DNA banks for criminal investigations[14] or "problems that might arise because of other

[12] For a helpful list of ethical tensions and issues in biobanking, including consent, ownership and IP, governance, public engagement, data-sharing, research access, security, privacy, benefit-sharing, commercialisation, discrimination, public good, cultural sensitivity and international harmonisation, see Cambon-Thomsen, A, et al, "Biobanks for genomics and genomics for biobanks" (2003) 4 *Comparative and Functional Genomics*, (6) 628-634; Caulfield, T "Biobanks and Blanket Consent: The Proper Place of the Public Good and Public Perception Rationales" at 209-226 Caulfield, T "Biobanks and Blanket Consent: The Proper Place of the Public Good and Public Perception Rationales" at 209-226

[13] Campbell, AV "The Ethical Challenges of Genetic Databases: Safeguarding Altruism and Trust" (2007), 18 *King's Law Journal*, 2 at 237-245.see also Chalmers D and Nicol D "Commercialisation of biotechnology: public trust and research" (2004) 6 *International Journal of Biotechnology* , 116-133; On the importance of public trust see Bovenberg J "Towards an International System of Ethics and Governance of Biobanks: A "Special Status" for Genetic Data?" (2005) 15 *Critical Public Health* 369-383. See also J Bovenberg "Inalienably Yours? The New Case for an Inalienable Property Right in Human Biological Material" (2004) 1 *SCRIPT-ed* 545.

[14] See Chalmers, D (Ed) *Genetic Testing and the Criminal Law* (ed) UCL Press London 2005. On legislation, see, for example, *Criminal Investigations (Blood Samples) Act* 1995 authorizing New Zealand's national DNA databank. For a UK perspective see the forthcoming report from the

utilisations, for civil or criminal purposes or for employment or insurance"[15] This chapter focuses on the legal responsibilities and obligations for biobank administrators and researchers in dealing with human tissue and data collections and biobank research participants.

1.1 What are Human Genetic Research Databases and Biobanks?

The OECD generally uses the term 'genetic databases' or 'Human Genetic Research Databases (HGRDs)' to describe large-scale collections of human tissue for research. The OECD Committee for Scientific and Technological Policy produced a Report on Human Genetic Research Databases that provides an excellent outline of the procedures to establish an HGRD, to collect and manage samples, to manage and govern databases and commercialisation aspects.[16] Apart from the terms HGRDs and biobanks, the Estonian Genome Project uses "genome database", the Latvian Genome Project uses "genebank" and the French National Ethics Consultative Committee uses "biolibraries".[17]. The term "biobank" is used in this sense and is largely synonymous with the term "human genetic research database". All involve the storage of human tissue.[18] For this reason, genetic registers[19] of personal and family genetic information and histories are usually not included in a discussion of HGRDs because they generally do not require any collection or storage of human tissue.

Nuffield Council on Bioethics, *The Forensic Use of Bioinformation: Ethical Issues*, September 2007.

[15] Ethical issues raised by collections of biological materials and associated information data;"biobanks' and "biolibraries"Opinion 77, Comité consultatif national d'éthique pour les sciences de la vie et de la santé, France, 2003 at 3 www.ccne-ethique.fr/english/start.htm

[16] OECD Committee for Scientific and Technological Policy: Working Party on Biotechnology *Tokyo Workshop Report. Human Genetic Research Databases: Issues of Privacy and Security. DSTI/STP/BIO* (2005) 14.

[17] Ethical issues raised by collections of biological materials and associated information data;"biobanks' and "biolibraries"Opinion 77, Comité consultatif national d'éthique pour les sciences de la vie et de la santé, France, 2003 http://www.ccne-ethique.fr/english/start.htm

[18] For a discussion of terminology, see Tutton, R and Corrigan, O, *Genetic Data Bases: Socio-Ethical Issues in the Collection and Use of DNA* Routledge London2004 at 2-4.

[19] Special health registers may include the Perinatal Registers, Cancer Registry and Mental Health Register. Some registers may be governed under specific legislation,which defines the type of data to be collected, the method of collection,and restrictions on its use and availability.

However, a distinction can be drawn between the generic OECD term HGRDs and biobanks. In the case of HGRDs, many existing collections of human tissue were developed primarily for diagnostic and clinical purposes (without consideration of research or with research later considered as a secondary purpose). Moreover, many HGRDs were developed for specific limited research purposes only with specific and limited consent regimes. There are, therefore, some unique considerations in relation to research using existing tissue collections.[20] In contrast, biobanks have been established generally with the specific aim of conducting research. Biobanks have also been established with careful efforts to ensure that participant's consent has been obtained to cover research generally including variations to the original purpose for future research. In this sense, if there is a difference between the two terms "HGRD" and "biobanks", a biobank tends to refer to a collection of human tissue, specifically created for research. However, the term "biobank" is often used interchangeably with HGRD to describe any collection of human tissue, which can and is used for research purpose. Both HGRDs and biobanks have the twin goals of facilitation of genomic research balanced with the protection of the welfare of the biobank sample contributors[21].

1.2 Genetic research and Privacy

Genetic tests and research can provide information not only about a person's genes, but also information about the person's parents, siblings and children and even cousins and other more distant blood relations[22]. For this reason some forms of genetic information have:

1. predictive potential;
2. implications for family members; and
3. potential to stigmatise.

[20] See section 3 below.

[21] See National Bioethics Advisory Commission Report Research involving Human Biological Materials: Ethical Issues and Policy Guidance Vols 1& II Bathesda, Maryland August 1999 http://www.georgetown.edu/research/nrcbl/nbac/pubs.html. See also National Bioethics Advisory Commission Report Ethical and Policy issues in Research involving Human Participants Vols 1& II Bathesda, Maryland August 2001 at http://www.georgetown.edu/research/nrcbl/nbac/human/overvol7.html.

[22] Or possibly unrelatedness in the case of, say, parentage testing.

Genetic research has aroused specific privacy concerns. There are community concerns that personal information disclosed in a genetic research project may be divulged to others, such as insurance companies or employers, to the detriment of not only the research participant but also the family members and communities that share the participant's genetic profile. Such distinctions are critical in the design, conduct and reporting of human genetic research and pharmacogenomic studies. The protection of privacy of genetic information was the driver behind the joint Australian Law Reform Commission and Australian Health Ethics Committee Report, *Essentially Yours*.[23] This Report examined personal genetic information privacy in the context, amongst others, of anti-discrimination, genetic testing, health service delivery, insurance, employment, law enforcement and parentage testing

2 COLLECTION OF NEW SAMPLES FOR BIOMEDICAL RESEARCH

2.1 Governance of a Biobank

The establishment of a biobank is a complex task that will involve negotiations with health officials, researchers, governing institution(s), research funding agencies, health consumer/ community organizations and ethics experts. Biobanks can be "staggeringly expensive"[24] to establish and operate. Some biobanks have been established by national legislation setting up an operating company structure [25] or using the structure of a foundation[26] (rather than a company). For example, the Estonian database is owned and controlled by the Estonian Genome Project

[23] *Essentially Yours: The Protection of Human Genetic Information in Australia Report* 96 2003.

[24] Greely H quoted in R Longtin "Canadian Province seeks control of its genes' (2004) 96 *Journal National Cancer Institute* 1567-69. There are also critics of biobanks who question their methodological soundness and research value.

[25] *Health Sector Database Act*, 1998 (deCODE Genetics). The Icelandic Supreme Court November 27, 2003, judgment No. 151/2003 suggested that the 1998 Health Sector Database Act might be unconstitutional. In 2000, the *Act on Biobanks* No. 110/2000 was introduced for the "collection, keeping, handling and utilization of biological samples from human beings".

[26] Estonia: *Human Genes Research Act*, 2000

Foundation. In addition, some countries have enacted specific biobank legislation.[27] As biobanks will involve public benefit research, the UK Biobank is managed under the structure of a charitable company[28] with an independent Ethics and Governance Council which is an independent body charged with oversight of UK Biobank and to monitor and advise on UK Biobank's compliance with the Ethics and Governance Framework of the project [29] Similarly, CARTaGENE has an independent Institute for Population, Ethics and Governance. Some countries have established an oversight body reporting to the relevant government minister. The Scottish Executive has funded Generation Scotland, in large part, and has also established the Generation Scotland Advisory Board with an oversight function.[30]

Apart from considerations of structure, a biobank governing body will introduce guidelines[31] for the ethical operation of the biobank. The issue of participant consent to enrolment in a biobank is, and has been the most debated and vexed ethical question.[32] The governing body will introduce also standard operating procedures[33].

Biobanks are being established at regional, national and international levels[34]. At the regional level biobanks have been set up by the Karolinska Institutet (Sweden);

[27] Eg Sweden: *Biobanks in Medical Care Act* 2002 information may only be used for research purposes.

[28] A charitable trust may possibly be used, Winickoff D and Winickoff R "The Charitable Trust as a Model for Genomic Biobanks' (2000) 349 *N Eng J Med* 12 at 1180-1184. See comment in Boggio A " Charitable Trusts and Human Research Genetic Databases" (2005) 1 *Genomics Society and Policy* 41-49.

[29] See UK Biobank, Ethics and Governance Framework, Version 2.0 Wellcome Trust and Medical Research Council and Department of Health UK, July 2006 at 16-18 http://www.ukbiobank.ac.uk/ethics/egf.php

[30] http://129.215.140.49/gs/GGSAB.htm

[31] See for example, OECD Working Party on Biotechnology *Draft Guidelines for Human Genetic Research Databases* DSTI/STP/Bio(2007)17/REVI, Paris, July, 2007; Trouet, C "New European guidelines fort he use of stored human biological materials in biomedical research" (2003) 30 *Journal of Medical Ethics* 99-103

[32] Campbell, AV "The Ethical Challenges of Genetic Databases: Safeguarding Altruism and Trust" (2007), 18 *King's Law Journal*, 237 at 239-233 and see section 2.5 below

[33] See, for example, *First-Generation Guidelines for NCI-Supported BioRepositories* April 2006, National Cancer Institute, National Institutes of Health, U.S Department of Health and Human Services
http://biospecimens.cancer.gov/biorepositories/First%20Generation%20Guidelines%20042006.pdf

[34] Kaye, J, Helgason, H, Nomper, A, Sild, T and Wendel I "Population genetic databases: A comparative analysis of the law in Iceland, Sweden, Estonia and the UK" L (2004) 8 *TRAMES* 1/2, 15-33

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CARTaGENE (Quebec),); the Western Australia project[35]; the National Heart, Lung and Blood Institute (NIH, USA); and the Centre for Integrated Genomic Medical Research (Manchester UK). At the national level, DeCode (Iceland) was the pioneer program that has been followed by GenomEUtwin (Finland); Estonian Genome; Danubian Biobank Foundation (involving six countries in Central Europe); KORA-GEN (Germany); LifeGen (Sweden); INMEGEN (Mexico); LifeLines (Netherlands); UK Biobank and Generation Scotland[36] that will enrol some 500,000 participantsts; and, the Lifelong Health Initiative (Canada)[37]. These regional and national biobanks have been specifically created for large-scale longitudinal genetic research projects. At the international level, the successor to the Human Genome Project, the International Haplotype Mapping Project is a collaboration between the USA, UK, Japan, Nigeria China and Canada to identify and compare genetic similarities and differences in collected human tissue samples to find genes that affect health, disease and medication responses.[38] Another international collaboration is emerging in the Public Population Project in Genomics (P3G)[39] that aims to facilitate collaboration between many national biobanks in a not-for-profit initiative to provide a public and accessible knowledge database for the international population genomics community. P3G will enable large-scale epidemiological studies to be undertaken. The regulation of biobanking has, or is being considered in a number of countries and by a range of research or regulatory organisations[40]. For

[35] For an account of Australian databases see Nicol D "Public trust, intellectual Property and human genetic Databases; the need to address benefit sharing' (2006) 3 *J of International Biotechnology Law* 89-103

[36] www.generationscotland.org and www.ukbiobank.ac.uk

[37] http://www.cihr-irsc.gc.ca/e/27982.html

[38] see http://www.hapmap.org/

[39] http://www.p3gconsortium.org/ The P3G motto is "transparency and collaboration'.

[40] Cambon-Thomsen, A, et al, "Ethical and legal aspects of biological sample banks: Synthesis, practical questions and proposals [Aspects ethiqués et réglementaires des collections d'échantillons biologiques: Synthèse, questions pratiques et propositions]" (2003) *Revue d'Epidemiologie et de Sante Publique*, 51 (1 II) at 121-126. Council of Europe, Steering Committee on Bioethics, Draft Recommendations on research on biological materials of human origin, Strasbourg, 28 November 2005; Opinion of the European Group on Ethics in Science and New Technologies to the European Commission, Ethical Aspects of Human Tissue Banking, 21 July 1998; Swedish Medical Research Council (MFR), Research ethics guidelines for using biobanks, especially projects involving genome research, June 1999; Report of the Bioethics Advisory Committee of the Israel Academy of Sciences and Humanities, Population-Based Large-Scale Collections of DNA Samples and Databases of Genetic Information, December 2002; ESRC Research Ethics Framework, Discussion Paper 2: Ethical issues raised by collections of biological materials and associated information data;"biobanks' and "biolibraries"Opinion 77, Comité consultatif national d'éthique pour les sciences de la vie et de la santé, France, 2003 The

example, the German National Ethics Council and the French National Consultative Ethics Committee for Health and Life Sciences have produced a joint Declaration of the need for a regulatory framework to ensure the development of research balanced with the protection of the individual. The Australian Law Reform Commission (ALRC) published *Essentially Yours: The Protection Of Human Genetic Information*, which recommended changes to the regulation of databases and genetic research in general.[41] In the UK, both UK Biobank and Generation Scotland have developed ethics and governance frameworks[42] to define the scope and limits of the projects nd this has been supplemented with specific human tissue legislation[43].

Once a decision to proceed has been taken, a governing body will be appointed and the governance arrangements instituted. An institution establishing a biobank must establish governance structures appropriate for and consistent with the primary research focus[44], including a separate independent ethics review board[45], to scrutinise and assess the ethical acceptability of the project. The governance

international dimension to research ethics: the significance of international and other non-UK frameworks for UK social science, April 2004; Department of Health & Human Services, Public Health Service, National Institutes of Health, National Cancer Institute, 133rd National Cancer Advisory Board, Summary of Meeting, February 16-17 2005; ESRC Economic & Social Research Council, Research Ethics Framework (REF), Discussion Paper 2, April, 2004; Working Group on DNA and Epidemiology (TUKIJA) of the National Advisory Board on Health Care Ethics (ETENE), DNA Samples in Epidemiological Research, 26 August 2002; Dr Beata Scholtz, Debrecen Clinical Genomics Center, Biobanks and Scientific Research; German National Ethics Council, Biobanks for Research, 2004.

[41] *Essentially Yours: The Protection of Human Genetic Information in Australia Report* 96 2003 Recs 18-1 to 18-3 and 14-1 to 14-5. Dr Francis Collins described the Report as "a truly phenomenal job, placing Australia ahead of what the rest of the world is doing, described this Report"Head, US National Human Genome Research Institute and Chair, Human Genome Project and International Haplotype Mapping Project News release during the XIX International Congress of Genetics Melbourne July 5-9 2003

[42] See www.generationscotland.org and UK Biobank, Ethics and Governance Framework, Version 2.0 Wellcome Trust and Medical Research Council and Department of Health UK, July 2006 at 10 http://www.ukbiobank.ac.uk/ethics/egf.php

[43] UK *Human Tissue Act* 2004.

[44] In this respect, there is a fundamental divergence between the commercial company structure and the research governance structure. Under a company structure, the accepted legal standard demands that the company owes its principal duties to the shareholders.

[45] The term Ethics Review Board (ERB) will be used generically in this chapter to refer to research ethics committees that approve human research proposals. These are nationall variously called, as examples, Institutional review Boards, human Research Ethics Committees, Local Ethics Review Committees. All have a broadly similar composition, including community members, lawyer, religious/ethicists member; researcher with no affiliation with the research project to be considered;; and, independent chair.

standards will cover confidentiality and privacy and the management and administration processes of the biobank with transparency and accountability.

Review of Governance. Governance and ethical standards in research are not static. Attitudes of today on standards for privacy and consent cannot be assumed to apply to later decade. It is important that the governance arrangements for biobanks are reviewed on a regular basis to ensure compliance with developing governance, ethical and legal standards[46]. These reviews should be conducted with opportunities for community and participant dialogue.

2.2 Public Trust and transparency

The governance structure for biobanks should enable public scrutiny of processes and promote opportunities for public input.[47]The research governance arrangements for biobanks should include public transparency procedures that allow public scrutiny and encourage public trust. For example, the funders[48] of the UK Biobank have appointed an independent Ethics and Governance Council (EGC) to monitor and advise on the the operations of the UK Biobank. Annual reports from both UK Biobank and the EGC are published and available publicly. The EGC also holds public meetings on its activities and publishes the minutes of all of its deliberations.[49]Any specific guidelines or changes in operating procedures should be notified publicly and provide opportunities for public input.[50] Public Trust in biobank research is widely accepted as an essential aspect of biobank governance.[51]

[46] Gibbons, SMC, Kaye, J "Governing Genetic Databases: Collection, Storage and Use" (2007),18 *King's Law Journal*., 201-208.

[47] R Tutton "Constructing Participation in Genetic Databases: Citizenship, Governance, and Ambivalence" (2007) 32 *Science Technology and Human Values* 170-195.

[48] The Medical Research Council, the Wellcome Trust and the Health Department.

[49] http://www.egcukbiobank.org.uk/meetingsandreports/index.html

[50] In Australia there is a statutory requirement, under the *National Health and Medical Research Council Act*, 1992, for two stages of public consultation before the publication of ethical guidelines for medical research. Similarly, in GMO licensing compulsory public consultation at the application and assessment stages are required, *Gene Technology Act*, 2000 S 52).

[51] Campbell, AV "The Ethical Challenges of Genetic Databases: Safeguarding Altruism and Trust" (2007), 18 *King's Law Journal* 2 at 227-245 and Hansson M "Building on Relationships of Trust in Biobank Research" (2005) 31 *J Med Ethics* 415-418. The National Institutes of Health, National Institute of General Medical Sciences (NIGMS), Human Genetic Cell Repository in the Coriell Institute, has produced a *Policy for the Responsible Collection, Storage and Research Use of Samples from Named Populations*, 2004. Note the Nolan Principles of Public Life covering

Public engagement has been a major feature of the development of major public biobanks.[52]

2.3 Technical Considerations

There are a number of technical requirements for an effective, secure and ethical biobank system[53]. Some of these can be noted. First, because health data and genetic information are "sensitive" personal information, this information should be protected by encryption codes and only accessible to properly authorised biobank employees and researchers under strict conditions[54]. Computing systems must not only be efficient and reliable, they must secure confidentiality and privacy of the information derived from the samples. This is a technical as well as an ethical issue. In this respect, a number of privacy enhancement information technology systems (PETs) are being developed. The computer industry and researchers have invested considerable time and energy in developing specific privacy enhancement technologies (PETs) to protect personal privacy, prevent unauthorised access to this information and, most importantly, to enable authorised access to information particularly for authenticating and checking information. Secondly, biobank laboratories and collection and testing facilities must comply with prescribed national accreditation standards[55]. Thirdly, the sample collection and storage processes must be quality assured to ensure that the collection, handling, storage,

responsibility, merit, independent scrutiny, equal opportunities, poverty, openness and transparency and proportionality. Office of Science and Technology, see www.ost.gov.uk/policy/advice/copsac/annex.htm.

[52] See OECD Creation and Governance of Human Genetic Research Databases (2007) particularly Chapter 3.5 *Public Engagement In the Establishment of a Population Database.*

[53] *First-Generation Guidelines for NCI-Supported BioRepositories* April 2006, National Cancer Institute, National Institutes of Health, U.S Department of Health and Human Services http://biospecimens.cancer.gov/biorepositories/First%20Generation%20Guidelines%20042006.pdf INTERNATIONAL SOCIETY FOR BIOLOGICAL AND ENVIRONMENTAL REPOSTITORIES (ISBER). "Best Practices for Repositories I: Collection, Storage, and Retrieval of Human Biological Materials for Research" (2005) 3 *Cell Preservation Technology* 1, 5-48.

[54] This is not to underestimate the complexity of information technology reliability and the sometimes exaggerated claims about the new information technology era, see Blumenthal, D and Glaser, J "Information technology comes to medicine" (2007) 356 *N Engl J Med* 24; 2527-2534

[55] Increasingly, national accreditation standards align with international standards developed by bodies such as the International Organisation for Standardisation (ISO). 'Global integration [through the facilitation of world trade by the WTO] is also forcing greater use of international Standards, with a concomitant reduction in the need for national Standards, Ministry of Economic Development *Review of New Zealand's Standards and Conformance Infrastructure* Wellington NZ September 2005 at 36.

processing, access and use of any samples are not tainted by human or process error. Fourthly, beyond the legal requirements for privacy and confidentiality are the technical issues of the number of data points to be collected in relation to each individual sample and then the actual coding of the collected sample. These technical decisions not only provide assurances of the authenticity of the privacy of the collected sample but also, equally importantly, determine the degree of interchangeability of data between biobanks wishing to conduct international research projects.[56]

Finally, industry standards for biobanks are developing, through biobank networks[57] to answer concerns from a Rand Corporation study[58] about inconsistencies in the collection, storage and access policies of biobank.

2.4 Independent Control of Data and Samples

The control of the biobank samples and data should be under the control of a body or individual independent from the researchers seeking access to the data or samples. Reports[59]and academic opinion support this general and emerging principle. Biobank governance arrangements should include the appointment of an independent intermediary *between* the researcher and the data or samples. The principle of independent control is specific to the governance of biobanks. The important underlying idea of an independent intermediary is the introduction of a check and balance in the governance structure for the date and samples on the biobank. This idea of trusteeship has been described by the Ethics and Governance Framework of the UK Biobank as acting "as the *steward* (emphasis added) of the

[56] See OECD Creation and Governance of Human Genetic Research Databases (2007) at Chapter 3.4 *Privacy and Confidentiality*.

[57] In Australia and New Zealand, the voluntary, not-for-profit Australasian Biospecimen Network is developing standardisation advice http://www.abrn.net/

[58] Eiseman E, et al Case Studies of Existing Human Tissue Repositories: "Best Practices" for a Biospecimen Resource for the Genomic and Proteomic Era prepared for the National Cancer Institute National Dialogue on Cancer (Arlington VA: Rand Science and Technology).

[59] The Australian Law Reform Commission in Report 96, 2003 recommended that best practice in genetic research involving genetic databases require the appointment of an independent intermediary between the researcher and the data and samples (a gene trustee) to protect the privacy of samples and information. Above note 14, Rec 16-1

resource, maintaining and building it for the public good in accordance with its purpose".[60]

2.5 Information and consent procedures for living donors

The collection of human tissue samples must be carried out in accordance with legal and accepted ethical standards, particularly the informed consent of the sample donor. The German National Ethics Council Opinion[61] addressed the consent issue and considered that it is essential that explicit information be given to those depositing tissue.

Consistent with established international standards for research generally, consent procedures will emphasise the provision of explicit information to participants, opportunities for further explanation of the information and time to understand the information.

Consent. The diverse aspects of the consent process for involvement in a biobank demands that the consent be informed, voluntary and written. Accordingly, the elements of proper consent for involvement in the biobank should respect participant autonomy[62] and include participant information, understanding and voluntary consent to the following[63]:

- Relevant risks and benefit, if any.
- The types of samples and data to be collected and stored.

[60] http://www.ukbiobank.ac.uk/ethics/egf.php. See also the "custodian" proposal by the Ireland Law Reform Commission *The Establishment of a DNA Database* Report78-2005 at Chapter 4 This principle will involve changes in practice and organisation for researchers and for some groups such as hospital-based pathologists

[61] Nationaler Ethikrat , *Opinion on Biobanks for Research* Berlin 2004.

[62] See generally, Caulfield, T "Biobanks and Blanket Consent: The Proper Place of the Public Good and Public Perception Rationales" (2007) 18 *King's Law Journal* at 209-226 and Campbell, AV "The Ethical Challenges of Genetic Databases: Safeguarding Altruism and Trust" (2007) 18 *King's Law Journal* at 227-245

[63] See OECD Working Party on Biotechnology *Draft Guidelines for Human Genetic Research Databases* DSTI/STP/Bio(2007)17/REV1, Paris, July, 2007 , Principles 5A-5H, best practices 5.1-5.9 and annotation para 27

- Research may also disclose information about family and relations and wether this will be communicated (see below).
- The nature of the intended research to be undertaken.
- Research projects and purposes (and the data derived) may change to *other* future research.
- Policy on sharing samples and data with other research organizations.
- Policies, guidelines and procedures for access by researchers to data/samples.
- Permission to collect other data from health-relevant records.
- Procedures for later re-contact.
- Arrangements for privacy security and confidentiality, including restrictions of release to insurers and employers.
- Anonymisation procedures and restrictions on re-identification.
- Feedback of research results and how they will be reported.
- The right to withdraw.
- Arrangements for the data/samples in the event of incapacity or death.
- Policy on benefit-sharing
- IP prospects
- Potential commercial involvement, and
- Absence of any personal financial gain for any participant[64]

Consent is a *process* that must ensure that proper informed and voluntary consent is obtained. The rights of sample donors must be clearly set out in the consent form to be signed before donating the sample. These rights include the voluntary nature of the consent, the right to obtain one's own information and the right to withdraw from the database. Proper consent may extend to re-contact by the biobank to collect new information or tissue/data for research in the future[65]. Consent in the

[64] Similarly, the HUGO Ethics Committee *Statement on Human Genomic Databases* in December 2002 declares that human genomic databases are a public resource (1(b)) and all should have access to the benefits of such databases (1(c)) declared that individuals should have choice with regard to donation storage and use of the sample and information derived from it. The participants were also to be informed of a degree of indentifiability and the possibility of information from the database might be shared with other researchers in other countries or commercial entities.

[65] See UK Biobank, Ethics and Governance Framework, Version 2.0 Wellcome Trust and Medical Research Council and Department of Health UK, July 2006at 6-11

case of biobanking goes beyond the legal form of the original consent and raises wider issues of the public interest and public good. Any discussion of privacy and autonomy raises issues of human rights and the principle of human dignity that, it has been argued, underpins human rights provisions in national constitutions and international conventions.[66]

The consent process must also recognise and respect cultural, social and religious differences. National research codes generally include special guidelines for indigenous communities. So the Canadian Institutes of health research guidelines[67] provide explicit consent is always required and that the transfer of data and samples also requires consent of the other original parties.[68]. In such cases consent may be required from the community and/or its leaders. Care in this type of research is essential to avoid some of the controversies that accompanied the earlier Human Genome Diversity Program (HGDP)[69] that aimed to construct the history of development, migrations and expansion of human population. The HGDP encountered considerable opposition and suspicion from indigenous peoples.[70]

Consent to future research Biobanks are established with the express aim of conducting *long-term* research where human tissue collected and the data derived will be stored and used for future research. Whether samples and data can be used for a particular future research project depends on the participant consent, that may be at three distinct levels:[71]

[66] Beyleveld, D and Brownsword, R *Human Dignity in Human Ethics and Bio-law* OUP 2001; see also Brownsword, R "Bioethics Today, Bioethics Tomorrow, Stem Cell Research and the Dignitarian Alliance (2003) 17 *Notre Dame Journal of Law Ethics and Public Policy* 15

[67] CIHR *Guidelines for Health Research involving Aboriginal People* May 2007 at http://www.cihr-irsc.gc.ca/e/documents/ethics_aboriginal_guidelines_e.pdf

[68] Ibid Article 12.2. See also Article 12.3 Secondary use of data or biological samples requires specific consent from the individual donor and, where appropriate, the community. However, if the research data or biological samples cannot be traced back to the individual donor, then consent for secondary use need not be obtained from the individual .

[69] See R. Calderon "The Human Genome Diversity Project: Ethical Aspects" (1996) 4 *Law and the Human Genome Review* 107; and, J. Fleming "Ethics and the Human Genome Diversity Project" (1996) 4 *Law and the Human Genome Review* 141.

[70] See extracts from *Declaration of Indigenous Peoples of the Western Hemisphere Regarding the Human Genome Diversity Project* (1996) 4 *Law and the Human Genome Review* 209.

[71] These levels of consent are specified on general research ethics guidelines (eg Australia *National Statement on Ethical Conduct in Human Research* 2007) or specific biobank guidelines (eg UK Biobank, Ethics and Governance Framework, Version 2.0 Wellcome Trust and Medical Research Council and Department of Health UK, July 2006 at 9-10)

a) Limited /specific consent for research for the use of the biospecimen for a specific project, or
b) Qualified/follow-up consent where a participant wishes to be contacted in the future if there is to be any extension or substantial variation from the original research project, or
c) Full/unspecified consent enabling the biospecimens to be used for all research and any future research.

The first level of specific consent is familiar and usual in medical research generally, and requires no comment.

At the second level, the participant consents to a specific project and consents to be recontacted for future long-term research. This type of consent may be referred to as "re-consent" or "future/ follow-up consent" and may arise in circumstances such as:

- To collect new/update information or samples,
- To seek consent for new uses or research not within the exiting consent.

In these cases, an Ethics Review Board (ERB) would review the original participant consent. The ERB must be satisfied, after proper consideration of the information provided to the participant and the consent given, that the participant has given permission to researchers to obtain future/ follow-up consent for future research.

Thirdly, full/unspecified consent sometimes referred to as "broad" [72] or "blanket" requires full information to and voluntariness of the participant. Here the biobank has consent for approved research projects but also for the use of the tissue/data for research in the *future*. Such consent must be properly and effectively obtained for all *future* research purposes. This type of consent is not common in health research and is the subject of continuing debate and some controversy.[73] So, there have been suggestions that the uniqueness of long-term commitment to a biobank may require some form of follow up (re-check) and periodic re-consent to ensure that the

[72] Hansson M "Should Donors be Allowed to Give Broad Consent to Future Biobank Research?" (2006) 7 *The Lancet Oncology* 266-269.

[73] Caulfield, T "Biobanks and Blanket Consent: The Proper Place of the Public Good and Public Perception Rationales" (2007),18 *King's Law Journal*, 2 at 209-226.

intention, understandings and voluntariness of the original consent continue.[74] For a valid broad/unspecified consent, there must be specific reference and mention in the original participant consent, to the use of the stored tissue/data collected *for one purpose* and the data derived can be stored and used for *other* future and unspecified research.

In all cases, participant consents must be reviewed on an on-going and routine basis that the biobank protocols ensure that the collection, use, storage and release of information are consistent with the actual consent given.

Health Related Information Biobank research will involve health and genetic research that has the potential to reveal medically relevant information about the health or future health of participants and possibly, participant's offspring or relations. It is essential that the research project include a clear policy on whether such information will be disclosed to the participants and the procedures to be followed for disclosure[75]. Consent processes should clearly communicated in writing to the participant at the recruitment stage whether health relevant information will or will not be, disclosed to the participant, participant's off-spring or relations.[76]

2.5.1 Competent adults

Recruitment into a biobank should ensure the *voluntariness* of consent and participation in conformity with general ethical principles and specific information above. Recruitment into a biobank should ensure non-discrimination[77] and the voluntariness of consent and participation in conformity with accepted research

[74] See Kaye, J "Abandoning Informed consent: The Case of Genetic Research in Population Collections" in Tutton, R and Corrigan, O, *Genetic Data Bases: Socio-Ethical Issues in the Collection and Use of DNA* Routledge London2004

[75] An important consideration is whether a qualified genetic counselor will disclose the information or whether such a counselor will be available to explain the significance of the results.

[76] Johnston, C and Kaye, J "Does the UK Biobank have a Legal Obligation to Feedback Individual Findings to Participants?" (2004) 2 *Medical Law Review* 239-267 argue that, in the case of the UK and other EU countries, there may in fact, be not only an ethical duty to disclose but also a legal duty by Article 2 of the *European Convention on Human Rights*

[77] The Council of Europe's 'Convention on Human Rights and Biomedicine' provides an Article 11 that "any form of discrimination against a person on grounds of his or her genetic heritage is prohibited".

ethics principles[78]. Many biobanks, such as the UK Biobank, have decided to concentrate on the recruitment of competent adults in the higher age groups.

2.5.2 Incompetent adults

There may be advantages for the inclusion in research of incompetent adults, suffering from cognitive impairment, intellectual disability or mental illness because they suffer from specific and hereditary genetic diseases that may be better understood through long-term research on their disease or disorder. However, many biobanks are not recruiting incompetent adult participants. The inclusion of incompetent adults in research (including others highly dependent on medical care or dependent or unequal relationships) is governed by legislation or research codes in all countries.[79] Broadly, these guidelines establish that:

- Special considerations and responsibilities attach to incompetent adults in research
- The research project and ethical approval should pay due regard to the best interests of the incompetent adult.
- Consent procedures and ethical review must address these special considerations and responsibilities for each specific research project.
- Ethical review should recognise that some incompetent adults may have some level of understanding of the research project, but not to provide consent.
- There should be no harm to the incompetent adult's safety and emotional psychological security.
- The research project should not involve any more than low risk (which is usually the case with biobanks) to the incompetent adult.
- The research project should involve a research question that could not be carried out on other competent research participants

[78] UK Biobank, Ethics and Governance Framework, Version 2.0 Wellcome Trust and Medical Research Council and Department of Health UK, July 2006at 5-6 provides that the selection process reflects inclusion of a wide variety of participants from minority groups and reflecting socially diverse cultural and functionally incapacitated groups

[79] See, for example, Chapter 4.5: People with a Competent Impairment, an Intellectual Disability, or a Mental Illness, *National Statement on Ethical Conduct involving Human Research* 2007 Australia.

- The guardian or other required legal representative's consent must be obtained.

2.5.3 Children

The practice of recruitment of children is variable between biobanks. The issue is no settled practice norm. Some studies are specifically aimed at children[80] and some biobank studies have decided not to recruit children as participants others will recruit. For example, the trans-genomic research in the African Diaspora (TgRIAD) has been implemented by the Howard University National Human Genome Centre to study diseases common amongst African Americans and other populations of Africa and the Caribbean.[81] This study will recruit whole households, including children. In the case of the Latvian legislation, the inclusion of children is permitted.

There may be considerable advantages for the inclusion of children in research. The inclusion of children is likely to assist in research into genetic diseases affecting the young and in understanding the development of late onset genetic diseases and other health problems from childhood to maturity. Similarly, the inclusion of children in research is governed by research codes in most countries.[82] Broadly, the guidelines in these codes establish:

- That special consideration and special responsibilities be attached to child research
- That there is a requirement that consent procedures and ethical review must be developed for the specific research project.
- That children have developing levels of maturity from being unable to understand the research project, to understanding some other relevant information, to understanding information but not being old enough to provide proper informed consent.

[80] The British Avon Longitudinal Study of Parents and Children (ALSPAC), http://www.alspac.bristol.ac.uk/welcome/index.shtml and the Australian Growing Up in Australia - Longitudinal Study of Australian Children http://www.aifs.gov.au/growingup/ are examples

[81] Section 2.1.7 OECD Creation and Governance of Human Genetic Research Databases (2006) available at http://www.oecd.org/document/50/0,3343,en_2649_34537_37646258_1_1_1_1,00.html)

[82] See, for example, Chapter 4.2: Children and Young People, *National Statement on Ethical Conduct in Human Research* 2007 Australia.

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- The research project should not involve any more than low risk to the child (by and large in biobank inclusion there should be no more than low risk).
- There should be no harm to the child and the child's safety and emotional psychological security and wellbeing should be included in the signed consent and conduct of the research.
- Parental or guardian consent should be obtained, and
- Overall, the project and ethical approval should pay due regard to the best interests of the child (even though there may be no direct benefit).

2.6 The role of ethical review boards in selection of appropriate information and consent procedures

Biobank participants will receive the range of information set out in section 2.5 before they are asked to consent to participate in the project. Once established, the biobank oversight body and Ethics Review Board (ERB) [83] will review and assess applications for access to its resource. The oversight body will ensure that the application complies with the purposes and ethical frameworks of the biobank and national legislation, guidelines and policies. Many biobanks have developed their own guidelines, supplementing national guidelines[84]. In addition, the oversight body or ERB will approve and monitor all research access applications. The role of the ERB is the traditional protection of the interests of the participants. When the project is independently reviewed for approval, the ERB will ensure that the project complies with the participants' consent, Apart from ensuring that the consent process addressed the consent matters set out at 2.5 above, the ERB should also ensure that the proposed project,

- involves a valid research question;
- addresses confidentiality and privacy

[83] See OECD Working Party on Biotechnology *Draft Guidelines for Human Genetic Research Databases* DSTI/STP/Bio(2007)17/REVI, Paris, July, 2007 . Principles 3B, 3C and best practice 3.2

[84] See, for example, UK Biobank, Ethics and Governance Framework, Version 2.0 uly 2006 and *First-Generation Guidelines for NCI-Supported BioRepositories* April 2006, National Cancer Institute, National Institutes of Health, U.S Department of Health and Human Services-http://biospecimens.cancer.gov/biorepositories/First%20Generation%20Guidelines%20042026.pdf

- involves whether collection and storage of new samples or data
- explains any changes to original access or release conditions
- involves research in other institutions, including overseas

2.7 Requirements for Privacy

Biobanks have legal duties to ensure the privacy and confidentiality of samples and data. The governing institution must assume responsibility for maintaining legal and ethical standards of confidentiality and privacy in the overall governance of its biobank Privacy legislation[85] is fairly standard in most countries because of the original OECD privacy principles developed in the early 1980s. Most countries have privacy legislation; some also have specific biobank legislation or other specific access to health records legislation.

Constitutional rights to privacy Rights to privacy are constitutionally guaranteed in some countries. These constitutional and legislative privacy rights are not absolute and are usually subject to exceptions and conditions determined by law. Constitutional rights to privacy, for historical reasons, usually apply to privacy of communications and have little relevance to modern biobanks[86]. Many countries do not include constitutional rights to privacy but have judicial recognition of such rights.[87]

Non-Discrimination and Freedom of Information Anti-discrimination laws may also

[85] For example, in Australian the *Privacy Act* 1988www.privacy.gov.au and http://www.privacy.gov.au/act/index.html that is similar to the New Zealand *Privacy Act*, 1993. See also Victoria: *Information Privacy Act* 2000 ; *Health Records Act* 2000 ; NSW: *Privacy and Personal Information Protection Act* 1998; *Health Records Information Privacy Act* 2002 ACT: *Health Records(Privacy and Access Act* 1997

[86] Belgium: Constitution recognizes the right of privacy (Article 22);r Estonia ;Constitution 1992 recognizes the right of privacy and data protection (Article 42); Finland:, Constitution of Finland The right to privacy (Section 10); Iceland: the 1944 Constitution was amended in 1995 for personal privacy (Article 72); Spain: Constitution recognizes the right to personal privacy; UK: The *Human Rights Act* includes a right of privacy.

[87] *Grundgesetz*, the German Constitution does not include a right to privacy. Similarly, Ireland and Canada, Singapore and India (Constitution 1950) have no express rights to privacy in their Constitutions However, in France; Constitutional Court ruled in 1995 that the right of privacy was implicit in the Constitution by decision 94-352DC du Conseil constitutionnel, 18 January 1995. So too in Japan in 1963 the Supreme Court recognized a right to privacy.
There is no explicit right to privacy in the United States Constitution

apply to some of the research and governance arrangements of biobanks. Biobanks should implement appropriate measures to avoid discrimination of stigmatisation of participants, their families and social groups.[88]Similarly, freedom of information legislation allows access to government-held information but are not, generally relevant to biobanks[89].

Data Protection the protections introduced in the computer age to protect personal data are important for biobanks and their sample donors. European nations must implement legislation to comply with the European Union *(EU) Data Protection Directive* (95/46/EC)[90]. The two major North American nations have complex data protection regulation arising from their federal arrangements.[91] Some Asian countries also have introduced data protection by legislation.[92]

Privacy legislation Privacy of personal information is an accepted legal and ethical principle. Originally, privacy law was aimed towards government record keepers and credit providers. By the 1990s greater concerns were being expressed about privacy in telecommunications and electronic record linkage including health information in general and genetic information in particular. Privacy law now has a

[88] See OECD Working Party on Biotechnology *Draft Guidelines for Human Genetic Research Databases* DSTI/STP/Bio(2007)17/REV1, Paris, July, 2007 , Principle 1E

[89] The original legislation was in the USA *Freedom of Information Act* (FOIA) 1966 that allows access to federal government records. See Thailand: *Official Information Act* (OIA) 1997 rights to government information.

[90] Belgium: : *Act concerning the Protection of Privacy with regard to the Treatment of Personal Data Files*, December 8, 1992 updated December 11, 1998; Estonia : *Personal Data Protection Act*, 1996; Finland: *Personal Data Act* 1999 : France: *Data Protection Act* 1978 *amended by Data Protection Act* 2004 for with the EU Directive ; Germany: 1997 Federal Data Protection Act (*Bundesdatenschutzgesetz* or BDSG) amended in 2002 to be in line with the EU Data Protection Directive; Iceland; 2000, *Act on the Protection of Individuals with regard to the Processing of Personal Data* for compliance with the EU Directive ; Ireland: *Data Protection Act*, 1998; Spain: *Data Protection Act* (LOPD) , 1999; Sweden: *Personal Data Act* (PDA) or *personuppgiftslagen* (PUL) 1998 ; Switzerland: *Federal Data Protection Act* 1992; UK: *Data Protection Act* 1998

[91] The *Privacy Act* 1985, Canada regulates the federal public sector. The *Personal Information Protection and Electronic Documents Act* 2000 (PIPEDA) applies to private sector commercial activities throughout the country, three provinces (Alberta, British Columbia and Quebec) that have enacted "substantially similar" provincial legislation. Four provinces have legislation for the protection of health information. Ontario (*Personal Health Information Protection Act* 2004), Manitoba (*Personal Health Information Act*), Saskatchewan (*Health Information Protection Act*) and Alberta (*Health Information Act*). USA: *Privacy Act* 1974 protects records of US government agencies

[92] E.g in Taiwan: *Computer-Processed Personal Data Protection Law* 1995.

major influence in the regulation of medical research generally and biobanks, in particular.

Privacy legislation applies across a range of principles from the collection through to the storage and use of data as follows:

- Principle 1 - Personal information should be collected for a lawful purpose and collected in a lawful and fair manner
- Principle 2 - Where personal information is collected for a record or solicited, the collector must ensure the individual concerned is aware of the purpose of the collection (at the time or as soon after as practicable), if the collection is authorised by law and the persons or agencies that could have the information disclosed or passed on to them.
- Principle 3 – The collection or solicitation of personal information should generally be relevant to the purpose for which it is collected.
- Principle 4 – Records of personal information should be stored with " such security safeguards as… reasonable in the circumstances" to prevent loss or unauthorised access, use or disclosure.
- Principle 5 – A record-keeper of personal information should take reasonable steps to enable persons to ascertain the existence of record about them and details about the nature and purposes of the record
- Principle 6 – Person should have access to records about them, except if restricted by law.
- Principle 7 – Record keeper to allow reasonable alteration of records containing personal information by the person and, if not, may attach a statement of correction, deletion or addition by the person.
- Principle 8 – A record-keeper to check that personal information accurate and up-to-date before use
- Principle 9 - A record-keeper cannot use personal information except for relevant purposes
- Principle 10 - Limits are placed on a record-keeper not to use personal information unless the person consents; authorised by law; there is reasonable belief of a threat to life or health; for law enforcement; or use is directly related to the purpose for which the information was collected.

- Principle 11 – Limits are placed on a record-keeper not to disclose personal information unless individual aware information likely to be passed on; individual consents; disclosure authorised by law; there is reasonable belief of a threat to life or health; for law enforcement; or disclosure is to an agency that will not use it for a purpose other than that for which the information was given.
-

These principles are general in most jurisdictions. Privacy is required and personal information must not be disclosed unless

- Person consents, expressly or by implication; or
- Disclosure necessary to lessen/prevent serious/imminent threat to person (life, health. safety) or serious threat to public health/safety; or
- Required or authorised by law; or
- Law enforcement

The major additions to this list have been the development of privacy principles dealing with-

- trans-border data flows; and
- sensitive information-exceptions

Sensitive information This last principle is important as "sensitive information" covers health information in general and biobank data in particular. Tissue samples, subject to genetic analysis provide *information* on sample donor are "sensitive information" and attract the privacy protection and enforcement procedures of the privacy legislation.

Enforcement Most privacy legislation is described as "light-touch" avoiding a strict enforcement regime in favour of the introduction of specific industry codes developed by the industries themselves and approved by an appointed Privacy Commissioner/ Ombudsman. Generally, complaints do not go to court but are dealt

with administratively by the Privacy Commissioner/ Ombudsman[93], according to the following steps

- Person may complain (no costs) to Privacy Commissioner
- Privacy Commissioner investigates/ conciliates
- Privacy Commissioner may impose fine or award compensation.

Access to information privacy legislation generally includes a right of access to and correction of personal information (see principles 6 and 7 above) In addition to the general privacy legislation; some countries (and states within federal systems) have supplemented the privacy with specific statutory rights to patients and particularly in relation to access medical records.[94] The Estonian legislation extends full access rights to sample donors.[95] There can also be court-authorized access to personal information where access is refused for improper reasons.

Ethical And Legal Duties of Confidentiality Finally, biobank staff are usually bound by codes of ethics, incorporated as terms of their contracts of employment. Similarly, researchers are usually bound by ethical and legal duties of confidentiality in MTAs [96]or in research access agreements. These duties require staff and researchers to maintain confidentiality of information acquired in the

[93] Finland: Data Protection Ombudsman (DPO); France: *Commission nationale de l'informatique et des libertes* (CNIL) enforces the Data Protection Act. Spain: Data Protection Agency (*Agencia Espanola de Proteccion de Datos*, or AEPD) enforces the LOPD; Sweden: monitored by the Data Inspection Board (DIB), *Datainspektionen*. ; Canada; Both the Privacy Act and PIPEDA are overseen by the independent federal Privacy Commissioner of Canada; New Zealand: Office of the Privacy Commissioner.UK: The Office of the Information Commissioner enforces the *Data Protection Act*; USA: There is no independent privacy oversight agency in the United States.

[94] For example, USA: *Protections for medical records are found in the Health Insurance Portability and Accountability Act* (HIPAA) of 1996. In April 2003, Standards for Privacy of Individually Identifiable Health Information (the HIPAA Privacy Rule) were introduced; Finland: *Act on the Status and Rights of Patients* 1993 and *Medical Research Act* 1999;; Sweden: Health and medical sector regulated by *Health Care Register Act* 1998 and *Patients' Records Act* 1985. DNA use in law enforcement. Chapter 28 of the Code of Judicial Procedure and the rules in the *Police Data Act* of 1998.

[95] Eg France genetic data, under the *Internal Safety Law* Loi n2003-239 , 18 march 2003 extended for the DNA National Computerized File of Genetic Data (*Fichier national automatisé des empreintes génétiques* or FNAEG).

[96] Eg "The Recipient will in no way attempt to identify or contact the person(s) associated with the biospecimen9s) that make up the MATERIAL under this Agreement. Furthermore, Recipient will not attempt to obtain or otherwise acquire any private identifiable information associated with the biospecimen9s) that make up the MATERIAL under this Agreement" Clause 8 Appendix A2-1 *First-Generation Guidelines for NCI-Supported BioRepositories* April 2006, National Cancer Institute, National Institutes of Health, U.S Department of Health and Human Services-http://biospecimens.cancer.gov/biorepositories/First%20Generation%20Guidelines%20042006.pdf

course of biobank work or research. Breaches of duties of confidentiality can lead to dismissal from employment. Where biobanks are established by legislation, the act usually includes a statutory offence for unauthorized disclosure of information[97].

2.8 Research Guidelines

The "hard law" privacy legislation is supplemented by "soft law" research guidelines and policies that establish ethical duties for privacy of information and data in research. The *Declaration of Helsinki* (1964 and subsequent revisions) is the international foundation for the common framework for the regulation of human experimentation and established the key pillars for ethical review in medical research (voluntary consent of the research participant; independent review of the project; assessment of the risk; involvement of competent researchers of integrity and research merit). These guidelines are contained in national codes of ethical conduct in research in most countries[98]. The trend in most countries is towards greater regulation of human research and away from earlier self-regulation.[99] Importantly, the approval processes of ERBs must ensure "... provisions to protect the privacy of subjects and to maintain the confidentiality of data"[100] be in place.

Overarching these national codes, most biobanks have special ethics and governance oversight frameworks in place that have been introduced in legislation[101] or in guidelines and policies. The OECD proposes it is best practice to

[97] E. g. Estonia, *Human Genes Research Act* 2001

[98] For example, *National Statement on Ethical Conduct in Human Research* 2007 Prepared by the Australian Health Ethics Committee under the relevant provisions of the *National Health and Medical Research Council Act*, 1992 (Cth) .

[99] Chalmers, D "Research Involving Humans: A Time for Change?"(2004) 32 *J of Law, Medicine & Ethics* (4) 583-495.

[100] This is the USA Common Rule formulation Department of Health and Human Services Policy for the Protection of Human research Subjects 45 CFR 46.111(a)(7). See also Bioethics Advisory Committee of Singapore Report on genetic testing and genetic research 2005 on privacy and the confidentiality at http://www.bioethics-singapore.org/resources/reports4.html. Japan published, *Guidelines for the Protection of Personal Information in Businesses that Use Human Genetic Information* in December 2004

[101] See for example, in Singapore, the *Human Tissue Research* (2002), *Genetic Testing and Genetic Research* (2005) and *Personal Information in Biomedical Research* (2007), The Bioethics Advisory Committee, Singapore (http://www.bioethics-singapore.org/resources/reports.html)

establish such an oversight body,[102] as was done by the UK Biobank Ethics and Governance Framework. Similarly, the Department of Health and Human Services, the National Institutes of Health and the National Cancer Institute[103] have developed jointly a comprehensive template set of guidelines, policies and procedures for biorepositories in the USA that support such oversight.[104]

2.9 Using biological material from deceased donors

Death of a biobank participant raises the issue of withdrawal from the biobank. Critically, the right to withdraw may become technically difficult after the data is anonymised. The UK Biobank has decided to exclude and not to enrol participants who express the view that they would want to withdraw in the event of death or incapacity.[105]

The consent process and any instruction of the participant determine the use of biobank data/samples after the death of the participant. The information provided and consent forms should state explicitly what may be done with the samples after death. These forms should be retained and available to ensure compliance with the actual consent. Generally, next-of-kin have no property in the tissue of a deceased and no rights of removal from a biobank, unless conferred and stipulated in the consent form. However, there may be some privacy interests that may be pursued.[106]

[102] See OECD Working Party on Biotechnology *Draft Guidelines for Human Genetic Research Databases* DSTI/STP/Bio(2007)17/REV1, Paris, July, 2007 , Principle 3B, best practice 3.1-5.9 and annotations paras 18, 19

[103] *First-Generation Guidelines for NCI-Supported BioRepositories* April 2006, National Cancer Institute, National Institutes of Health, U.S Department of Health and Human Services http://biospecimens.cancer.gov/biorepositories/First%20Generation%20Guidelines%20042006.pdf

[104] INTERNATIONAL SOCIETY FOR BIOLOGICAL AND ENVIRONMENTAL REPOSITORIES (ISBER). "Best Practices for Repositories I: Collection, Storage, and Retrieval of Human Biological Materials for Research" (2005) 3 *Cell Preservation Technology* 1, 5-48. http://www.isber.org/Pubs/BestPractices.pdf

[104] The most persuasive justification for these oversight bodies is assurance of public trust and confidence, rather than novelty of ethical, research or research governance questions (acknowledging comments from Professor Laurie)

[105] The UK Biobank has so decided "because this would reduce the value of the resource for research", Ethics and Governance Framework, Version 2.0, July 2006 at 11. See also OECD *Creation and Governance of Human Genetic Research Databases* (2007) at 92

[106] See *Ragnhildur Guomundotirv State of Iceland* 920030 Supreme Court of Iceland No151/2003. The Estonian act allows relatives access. . For comment, see Gertz, R "An Analysis of the Icelandic Supreme Court Judgment of the Health Sector Database Act", (2004) 1(2) SCRIPT-ed 241-258, available: http://www.law.ed.ac.uk/ahrc/script-ed/issue2/iceland.asp