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.nbm.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 Ethikraat , *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 Dome 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

[71] 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.

- 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/bionepositories/First%20Generation%20Guidelines%20042006.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/REVI, 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/bioreposistories/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/report4.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/REVI, 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 INTERNATIONAL SOCIETY FOR BIOLOGICAL AND ENVIRONMENTAL REPOSITTORIES (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 Guomundsdottir 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

2.10 Using biobank data for research

The biobank governing body will establish clear policies, guidelines and procedures, consistent with the governance aims of the biobank, for access by researchers to data/samples. First, access must be consistent with participants' consent and will require ERB approval and undertakings that privacy and confidentiality will be guaranteed. Secondly, biobanks will have privacy enhancement technology systems for anonymisation of data, including systems for re-anonymisation of tissue samples after later re-identification of a participant (provided consent permits such recontact for future research projects). Access by researchers will be recorded and may be granted under a licence setting out the duties and obligations of the researcher.[107]

Biobank governance arrangements will prescribe the proper and allowable research purposes for the data/samples (see also 2.7 above). Nevertheless, concerns exist about the possible misuse of biobank data focus on possible improper access to the data by enforcement authorities or, possibly private health care providers, interested in direct marketing. In addition, insurance companies, employers, litigants in paternity disputes or immigration departments could be interested in biobank records. As noted at 2.7 above, privacy legislation provides that information collected for one purpose should not be used for other purposes. While biobanks may not prevent access by law enforcement agencies, their governance arrangements should specify that access would be for approved research purposes and not for other purposes.

2.11 Transfer of samples and data within and between countries

Transnational Recognition of Research Ethics Approvals

[107] 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 14-16

It is also becoming common for data collections to be linked through formal exchange and co-operation agreements to facilitate research and to enable large-scale research and comparative work on the collaborating datasets. In these cases, the collaborating partner institutions should develop formal exchange agreements. These exchange agreements between collaborating institutions should also include reciprocal access and release agreements. Importantly, licences or materials transfer agreements (MTAs) should be in place and each MTA recorded[108] All access to and release of information from data collections should be strictly recorded so providing a guaranteed, continuous "chain of responsibility" [109] for all access and release dealings in relation to the storage, handling and use of body material and personal data. Access to and release of information must be able to be tracked and audited[110].

The Organization for Economic Cooperation and Development (OECD) *Guidelines on the Protection of Privacy and Transborder Flows of Personal Data.* 1980 was influential in the revisions of national privacy legislation to ensure conformity to standards for trans border flows of data.

The MTA should set out conditions on the processes for transfer of the data, data security, use and release of the data, approved research uses, intellectual property rights and duties, liability arrangements, termination and, finally, requirements for the data on completion of the project.[111] As a general ethical principle, a researcher

[108] See Appendix 2 'Material Transfer Agreement for Human Biospecimens" in 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/bionepositories/First%20Generation%20Guidelines%20042006.pdf

[109] The German National Ethics Council and the French National Consultative Ethics Committee for Health and Life Sciences a 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.

[110] See SECTION I. INTERNATIONAL SOCIETY FOR BIOLOGICAL AND ENVIRONMENTAL REPOSITITORIES (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

[111] *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/bionepositories/First%20Generation%20Guidelines%20042006.pdf
INTERNATIONAL SOCIETY FOR BIOLOGICAL AND ENVIRONMENTAL REPOSITITORIES (ISBER). "Best Practices for Repositories I: Collection, Storage, and Retrieval of Human Biological Materials for Research" (2005) 3 *Cell Preservation Technology* 1, 5-48.

should not transfer tissue or data to another research group unless an ERB has approved the research and the genetic material and data is provided in a form, which ensures that participants cannot be identified. Some national codes for ethical research recognise a system of centralised ethical review for multicentre research. Under these arrangements, guidelines usually allow the acceptance of a central ethical assessment or adoption of the decision of another research review committee. This avoids duplication and enables common monitoring and reporting responsibilities to be undertaken.

With the growth of biobanks and cross-border collaborations, there is a need for greater international harmonisation of regulation[112]. There is already considerable harmonisation between the codes of research guidelines of most nations[113]. The CIOMS *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, 2002 establishes standards but the operation of national codes often uncovers significant divergences in practice. International cooperation has already been well established with the international HapMap Consortium and the development of the P3G Consortium. In addition, statements of general principles are developing in the Human Genome Organisation (HUGO) *Statements on Human Genomic Databases on DNA Sampling: Control and Access*, and, *on the Principled Conduct of Genetic Research* and UNESCO's *International Declaration on Human Genetic Data* (2003), and *Declaration on the Human Genome and Human Rights*,[114]

2.12 Collaboration between academic and commercial partners

Biobanks have a primary public research focus. This does not preclude private companies that may apply, subject to conditions, to use biobank data and resources. The pharmaceutical industry is interested in biobanking with hopes that pharmacogenomic research may herald a new generation of medicines tailored to

http://www.isber.org/Pubs/BestPractices.pdf'

[112] Knoppers, BM, et al "Genomic Databases and International Collaboration" (2007), 18 *King's Law Journal*, 291-311; Knoppers, B 'Biobanking: International Norms' (2005) 33 *Journal of Law, Medicine & Ethics* 7; Kaye, J "Do we need a uniform regulatory system for biobanks across Europe?" (2006) 14 *European J of Human Genetics* 245-248

[113] See Chalmers, D "Ethical Principles for Research Governance of Biobanks" (2006) 3 *International Journal of Biotechnology Law* 221-230. See also, Quebec Network of Applied Genetic Medicine *Ethical Conduct of Human Genetic Research Involving Populations*.

[114] Promulgated by the General Conference of UNESCO at its 29th Session on 11 November 1997.

individual needs. If not individualised medicine, this research may enable better patient stratification thus achieving better patient outcomes from the drug administration. Commercial collaborations may arouse, in the words of the German National Ethics Council, "anxiety and distrust".[115] Similarly, the Australian Law Reform Commission public consultation process uncovered public scepticism about the continuing "heavy degree of commercialisation of [medical and genetic] research" and that people did not want their "altruism to lead to billion dollar profits for multinational pharmaceutical companies"[116] Recognising that commercialisation challenges public trust in science,[117] a policy of transparency and public engagement by biobanks in relation to their commercial activities is advisable. The Generation Scotland project is carrying out an on-going programme of public engagement, focussing especially on issues and concerns about commercialisation[118].

Commercialisation. Some biobanks have been established as research platforms to support both public and private research. Some of this research therefore may have commercial outcomes.[119] There is evidence of community concerns with commercialisation of research that must be tackled by demonstrating the public benefits that may flow from this research.[120] A distinction can be drawn between the intellectual property rights in the databases and intellectual property arising from research using these databases. In the former case, the European Union Directive on the *Legal Protection of Databases* (96/9/EC) provides that the ownership of the intellectual property in the database vests in the "maker" of the database, giving 50 years protection for work and costs in compiling, verifying and presenting data. So, the governing foundations of some biobanks (e.g. Iceland, Estonia and UK) establish that the intellectual property accruing from the creation and development

[115] Opinion on *Biobanks for Research* at 27.

[116] Cited in Weisbrot, D 'Public Conspiracy, Genetic Counselling and the Required Legal Infrastructure', Symposium on Taiwan's Private Project, unpublished paper ALRC Sydney, 8 August 2005 at p19

[117] Chalmers, D and Nicol, D (2004) "Commercialisation of Biotechnology: Public Trust and Research", 6 *Int.J.biotechnology* 116.

[118] See Generation Scotland website: http://129.215.140.49/gs/gpce.htm

[119] See OECD Creation and Governance of Human Genetic Research Databases (2007) Chapter 6 *Commercialisation Considerations*.

[120] Haddow, G, Laurie, G et al "Tackling community concerns about commercialization and genetic research: A modest interdisciplinary proposal" (2006) *Social Sciences & Medicine* (forthcoming)

of the database accrues to the biobank. In the case of intellectual property arising from research using these databases, the arrangements for access and use of the biobank data will set out the intellectual property arrangements. Generally, the biobank will expect some share of the IP rights with the researcher/research organisation . Generally, IP rights are clearly stated by the biobank to remain with the researcher/research organisation (or, in some cases shared with their assignees) and not with the participant.

Conflicts of interest Potential conflicts of interest must be audited and managed in collaborations and partnerships between commercial organisations and biobanks. The general principle of disclosure of interest is recognised in national codes for the responsible conduct of research[121]. There are also well-established policies of science and medical research journals requiring declarations of financial associations with commercial organizations before, and as a condition of, publication.

Ownership of samples. The question of ownership of body parts and tissue remains unsettled in both common and civil law jurisdictions[122]. The better view is that a biobank is trustee/steward of the samples for the purposes set out in the consent. In any case, the data created from the research will be owned by the researcher or subject to some special agreement between the biobank and the researcher. The sample donor does not have any claims in the eventual product of the research. Some biobanks have tried to clarify these positions. The UK Biobank states that participants "will have no property rights in the samples"[123] and this will be explained in the consent process. Similarly, the Estonian Genome Projects states that ownership to samples vests in the Project. This does not preclude the capacity of sample donors to have agreed rights of access to information or to withdraw from the project, or, in some cases, have the sample destroyed. Importantly, consent documents will clarify that the sample donor does not have and will not obtain any

[121] See as example, Australian Code for the Responsible Conduct of Research 2007.

[122] For a discussion of property and donor samples see J Bovenberg "Inalienably Yours? The New Case for an Inalienable Property Right in Human Biological Material" (2004) 1 *SCRIPT-ed* 545.

[123] The UK Biobank, Ethics and Governance Framework, Version 2.0, July 2006 Section A "Stewardship of Data and Samples at 14

intellectual property rights in the database, in research results or in any product arising from the research use of the biobank.

The commercialisation of biobank results is quite separate from the issue of fees for service. Many biobanks have a tiered pricing system for different researcher categories.

2.13 Public Dissemination of Research Results

As a general ethical standard, participants should be provided with information about the results of the research.[124] As a general accepted ethical principle, the results of research should normally be published and disseminated to contribute to the advancement of public knowledge.[125] Biobanks should commit to this principle and encourage research to be published in the scientific literature or in other ways that allow assessment and scrutiny of the results. The International Haplotype Mapping Project[126] and GenBank [127] accept this publication policy. On the other hand, where a biobank is operated as a private resource, for example by a pharmaceutical company, there may be policies or restrictions on publication and dissemination of results. [128]

2.14 Requirements regarding coding and anonymisation

[124] See for example, in Australia, *National Statement on Ethical Conduct in Human Research* 2007, Sec 1.5 "Research outcomes should be made accessible to research participants". However, with large-scale biobanks, such as the proposed 500,000 volunteers on the UK Biobank, such participant consent may become difficult and impractical. Some biobanks, and the UK Biobank is an example, of chosen, that they will not provide "participants with information, genetic or otherwise, derived from examination of the database or samples by research undertaken after enrolment". See UK Biobank *Ethics and Governance Framework* at 8. However, the initial laboratory analysis results will be provided to participants at the physical assessment preliminary stage.

[125] Australia, *National Statement on Ethical Conduct in Human Research*, Sec 1.3(d) " disseminating and communicating, whether favourable or unfavourable, in ways which permit scrutiny and contribute to public knowledge."

[126] The successor to the Human Genome Project, see http://www.hapmap.org/ Access attracts a "clickwrap" licence to protect the data from bogus patent claims.

[127] The Human Genome Project's public domain sequence data site at http://www.ncbi.nlm.nih.gov/Genbank/

[128] See generally, Chalmers D and Nicol D, "Commercialisation of Biotechnology: Public Trust and Research" (2004) *6 International Journal of Biotechnology* 116-133.

Privacy and confidentiality of data are critical for biobanks. Biobanks should have explicit policies about coding and data linking to sample donors to safeguard privacy and confidential handling of and access to the data. Standard operating procedures for biobanks will include explicit conditions for maintaining privacy by coding and de-identifying data.[129] The use of unique identifiers and security access codes for authorised users are essential. Computing programmes will also include password and other restricted access systems to limit or block data access only to authorized users.

National codes of research ethics distinguish generally between *identified, de-identified* and *re-identifiable* information but the use of these terms are not consistent and may pose difficulties for developing an international framework.[130]. In the latter, the tissue and data are coded, but the code can be reversed and the participant's identity revealed. The UNESCO *International Declaration on Human Genetic Data* (2003) adopts similar distinctions between "(ix) *Data linked to an identifiable person*: Data that contain information, such as name, birth date and address, by which the person from whom the data were derived can be identified; (x) *Data unlinked to an identifiable person*: Data that are not linked to an identifiable person, through the replacement of, or separation from, all identifying information about that person by use of a code; (xi) *Data irretrievably unlinked* to an identifiable person: Data that cannot be linked to an identifiable person, through destruction of the link to any identifying information about the person who provided the sample'

The NBAC referred to *unidentified samples* that can sometimes be termed "anonymous" human biological specimens; *unlinked samples* that can sometimes be termed "anonymised" because they lack identifiers or codes that can link a sample to an identified person; *coded samples* that can sometimes termed "linked" or

[129] *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 http://www.isber.org/Pubs/BestPractices.pdf

[130] See Knoppers, BM and Saginur, M "The Babel of genetic data terminology" (2005) 23 *Nature Biotechnology* 925-927; Elger, B and Caplan, A "Consent and anonymization in research involving biobanks. Differing terms and norms present serious barriers to an international framework". (2006) 7 *EMBO reports* (7) 661-666; [130] Knoppers, BM, et al "Genomic Databases and International Collaboration" (2007). 18 *King's Law Journal*, 291-311;

"identifiable" that link identified specimens to a code and then to personally identifying information; and, *identified samples* that include a personal identifier (such as a name or patient number) to link the biological information directly to the individual from whom the material was obtained[131].

2.15 Withdrawal of consent and its effect on research

Biobank standards, policies and procedures generally allow participants to withdraw from biobank studies and projects. This is consistent with accepted international ethical research standard requiring participants be free, at any time to withdraw consent and to withdraw from further involvement in the project. In the case of a biobank research, it will not be possible to withdraw data from previously completed studies. Therefore, the ethical (and possibly contractual) right to withdraw must be contextualised to biobanks and may involve withdrawal of consent, samples and data at different levels, depending on the consent and choice of the participant. These levels of withdrawal are:

- *No further contact* – with the participant directly but allowing retention and use of previously provided data/samples with permission to obtain health-relevant records.
- *No further access - allowing* retention and use by the biobank of the data/sample but no participant contact and no permission to obtain health-relevant records, or
- *No further use* – no further contact with, or information from, the participant, including the destruction of samples and health-related information (but not data already used),[132]

2.16 The completion of a project and its effect on samples and data

As a general principle, biobanks should have policies and guidelines dealing with the possibility of transfer, closure of assets and these should be communicated to the

[131] See National Bioethics Advisory Commission Report *Research involving Human Biological Materials: Ethical Issues and Policy Guidance* Vols 1& II Bathesda, Maryland August 1999 pp 16-17

[132] UK Biobank *Ethics and Governance Framework*, Version2.0 July, 2006 at 10 http://www.ukbiobank.ac.uk/ethics/egf.php

participants at the time of recruitment. Similarly, any variation in the arrangement for the maintenance or storage or stewardship of the data for samples should be communicated during the currency of the biobank.

3 USE OF PREVIOUSLY COLLECTED SAMPLES

Collections of human tissue[133] have been a common place in hospitals and specialist clinics from the 19th century when preservation techniques were introduced.[134]. In 1998, the former National Bioethics Advisory Committee (NBAC) estimated that there were more than 282 million specimens stored in the United States and further estimated that the accumulation rate from blood tests, surgery and other medical procedures was probably in the region of 20 million specimens per year.[135] This NBAC report outlined the types of existing collections of human tissues as follows

- Pathology samples - clinical/diagnostic purposes;
- Researchers'/ pharmaceutical company collections for unique/ longitudinal research studies;
- Newborn screening tests (Guthrie cards);
- Forensic DNA banks;
- Umbilical cord blood banks;
- Organ, sperm, embryo and now stem cell banks;
- Blood banks

To this list should be added specialised human tissue collections, particularly of cancer tissue, used for specialist research.[136] Each of these samples can be further

[133] See, Medical Research Council policy and guidance on human tissue: http://www.mrc.ac.uk/PolicyGuidance/EthicsAndGovernance/UseofHumanTissue/index.htm For example, the tens of millions of cervical cell samples collected each year are invaluable archival samples for research that can be linked to cancer registries, Arbyn, M et al *Methods in Molecular Biology* 2007 at Chapter 17 "Cervical Cytology Biobanks as a resource for Molecular Epidemiology'

[134] See R Scott, *The Body as Property*, Alan Lane, London 1981, Ch 1.

[135] National Bioethics Advisory Commission *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance* Vol I Maryland 1999 at 13-15. See comments in B Knoppers "DNA banking: A retrospective-prospective" in Burley J and Harris J *A Companion to Genethics* Blackwell Publishing 2002, 379-386..

[136] See generally, Knoppers, B, Laberge C and Hirtle, M, *Human DNA: Law and Policy International and Comparative Perspectives* Kluwer Law International The Hague, 1997

divided onto slides, paraffin blocks, frozen or formalin-fixed or extracted DNA. DNA test results from these divided samples forms another further data set.

3.1 Using samples and data without consent or without renewed consent

These collections of tissue and data, held in long-term storage, are often not covered by patient consent. However, it is common for these tissue collections, that were originally collected for clinical or diagnostic purposes, to be used for other undefined research. This is frequently the case with hospital pathology samples that were usually collected for routine diagnostic and clinical purposes but may now used for research. Historically, hospitals and other institutions holding tissue did not presume refusal, or implied refusal, of consent by patients but presumed, in the absence of consent that it was "consistent with good stewardship to allow reasonable and respectful use [in research] of such legacy tissue collections for the greater public good".[137] The debates about biobanking have focused discussion on how existing tissue collections may be best managed ethically recognizing that in such cases, the issue of participant consent may be problematic. Generally, most countries allow stored tissue to be used in research provided the project is scientifically assessed, approved by an Ethics Review Boards and the samples de-identified[138],

The distinction between these *existing* collections of human tissue and *future* collections developed specific research purposes is significant in law. Under existing privacy legislation discussed at 2.7, the privacy rules and principles restrict data and information from being used *except* for the purpose for which it was collected. In effect, this rule of privacy precludes the use of data and information for any *secondary* purpose.

[137] See the helpful discussion on this point in Bioethics Advisory Committee (BAC) in Singapore, Report on *Human Tissue Research* (2002) (http://www.bioethics-singapore.org/resources/reports.html) at paras 9.1 - 9.6). This Report interestingly describes existing collections as "legacy tissue"

[138] Ibid, BAC, Report on *Human Tissue Research* (paras 9.1 - 9.6) felt that it was unjustified to equate absence of consent with refusal of consent and therefore allowed research if the stipulated safeguards of IRB approval and anonymization were in place.

Waiver Of Consent The use of human tissue samples in existing collections for research purposes will usually be accompanied by the express consent of the participant. However, ethical approval for the research may be granted by an ERB, in the absence of express consent. In such case the ERB may waive express consent.[139] Where researchers propose to use existing collections for other *secondary* research purposes, national codes of research ethics generally allow researchers to apply to an ERB for approval of a project. In these cases, the ERB may *waive* the requirement for individual consent. Waiver of consent is not uncommon in epidemiological research and human tissue research. In such cases, ERBs may waive consent after carefully considering a number of factors. Generally, the most important factor is whether the public benefit interest[140] in the value of the research *outweighs* the private interest in personal privacy. The types of factors that will be considered are:

- the nature of existing consents relating to the collection,
- the justification presented by the researcher for the waiver,
- the extent to which it is impossible or difficult or intrusive to obtain specific consent;
- the proposed arrangements to protect privacy
- the extent to which the proposed research poses a risk to the privacy and well being of the individual;
- whether the research proposal is an extension of, or closely related to, a previously approved research project;
- the relationship of the project to an existing project
- the possibility of commercial exploitation of the sample;
- statutory provisions.
- most importantly, whether the public interest in the value of the research *outweighs* the requirements of personal privacy.

[139] Zaps, N et al "Waiver of Individual Patient Consent in Research: When do Potential Benefits to the Community Outweigh Private Rights?" (2007) 186 *Med J Aust* 88-90. See Australia, *National Statement on Ethical Conduct In Human Research*, Ch 2.3 on qualifying or waiving conditions of consent.

[140] Beyleveld D, "Data Protection and Genetics: Medical Research and the Public Good" (2007) 18 *King's Law Journal* 275-289

Where a research project is approved and allows the project to proceed without individual consent, the ethics committee may impose conditions on the methods for the data collection, use and protection. Most obviously, the ERB may require that the data be only accessed in a de-identified form. The access to the data may be restricted to certain researchers only. Certainly, the research data must only be used for the research purposes specified in the ethics approval and cannot be used for further research projects without a new ethics approval.

3.2 Role of Ethics Review Boards in selection of appropriate information and consent procedures

For existing collections, ERBs also have the traditional role, discussed at 2.6 above, of protection of the welfare of the sample contributors. The ERB has the usual role to scrutinise and assess the ethical acceptability of submitted research projects using the existing stored data and tissue and decide whether the project involves proper participant consent and ethical conduct before deciding whether a researcher is permitted to carry out the research.

4 SOLIDARITY, DIGNITY AND BENEFIT-SHARING

Biobanking research will involve large-scale population cohorts. The scale of this type of research will challenge traditional notions of individualistic research and many social ideas[141]. New ideas within the new trilogy of "solidarity', and "benefit-sharing' are emerging. So, the UNESCO *International Declaration on Human Genetic Data* (2003) aims "(a) ... to ensure the respect of *human dignity* and protection of human rights and fundamental freedoms in the collection, processing, use and storage of human genetic data, human proteomic data and of the biological samples ...in keeping with the requirements of equality, justice and *solidarity*..."(emphasis added)

[141] See Glasner, P Atkinson, P and Greenslade, H *New Genetics, New Social Formations* Routledge London, 2006

The term "solidarity' invites discussion about the social, family, political, legal and other factors that promote and maintain integration and trust in society. However, social solidarity in some countries can be used "in a somewhat stronger and more egalitarian sense, [to] require that so much help is provided that the gap between the under-privileged and the others is reduced or eliminated."[142] Biobanking is also about social trust, as discussed in section 2.2 above. This should require biobanks to consider ways in which public trust and engagement can be maintained to promote social solidarity. Similarly, there are deeper issues of the ethical principles to apply to biobanking research. In particular, there are genuine questions about a rigid adherence to individual rights and autonomy in the pursuit of the long-term public health goals of these research tools. Some conventional conceptions of consent may be difficult to accommodate. In some biobanking research[143]the traditional individualist principle of autonomy may be at odds with Asian[144], Melanesian and Pacific approaches to decisions made harmoniously within the family and group.

"Benefit Sharing' has found expression in guidelines prepared by UNESCO[145] and the Human Genome Organisation[146]. The principle of benefit sharing promotes the equitable distribution of benefits from research. UNESCO's *International Declaration on Human Genetic Data* is one of the most emphatic assertions of the principle and states that "benefits...from the use of human genetic data.... should be shared with the society as a whole and the international community." However, the principle is amorphous, particularly in relation to the operation of intellectual property protections and licensing[147]. Nevertheless, the principle encourages

[142] The European Group on Ethics in Science and New Technologies to the European Commission, General Report 2000-2005, *European Communities* 2005 at 3.

[143] See Thomasma, D, 'Proposing a New Agenda on Bioethics and International Human Rights' (2001) 10 *Cambridge Quarterly of Health Care Ethics* 299-310. The author proposes some procedural and substantive rules for the basis of an international multicultural bioethics (the rule of peaceful dialogue; rule against xenophobia; rule of respect for cultural pluralism; rule of the common good; rule of cultural apprehension; rule of respect for persons in context; and, rule of existential A Prioris).

[144] But see Jing-Bao Nie "The specious idea of an Asian bioethics" in Ashcroft R et al *Principles in health Care Ethics* John Wiley, 2007

[145] UNESCO *Universal Declaration of Bioethics and Human Rights* 2005.

[146] HUGO *Statement on Benefit Sharing* 2000.

[147] Chadwick, R and Berg, K, 'Solidarity and Equity: New Ethical Frameworks for Genetic Databases' (2001) 2 *Nature Reviews Genetics* 318; Simm, K, 'Benefit-sharing: an Inquiry regarding the Meaning and Limits of the Concept in Human Genetic Research' (2005) 1 *Genomics, Society and Policy* 29; Knoppers, BM,'Biobanking: International Norms' (2005) 33

researchers and research organisations to consider ways in which the benefits of the biobank research may be equitably distributed. It has been argued[148] that the rhetoric of this principle should be replaced with the implementation of appropriate and practical mechanisms for benefit sharing. Benefit sharing also arises in relation to the public or private benefits[149] to be derived from biobanking research and whether those benefits will accrue for the public good.[150] The French National Ethics Committee has commented that "resources used by private genomic laboratories, ...are not to be compared with those of public sector activity... private laboratories tend to keep their biological resources and their data banks to themselves. [and] the powerful bio-computerised genomic analysis tools are mainly developed in the private sector (using for the most part, for that matter, data and algorithms produced by the public sector). Such a situation could lead to a form of capture of this research domain by the private sector, and, because public and private strategies differ, the risk of impoverishment of scientific or conceptual quality".[151] This comment emphasises that there are general advantages from the public and private research that can lead to specific development of new health care products.[152]

5 CONCLUSION

Biobanks have the potential to enable a dramatic increase in the quantity of genomic research, as well as significantly improving the quality of the research

Journal of Law, Medicine & Ethics 7; D Nicol "Public trust, intellectual *Property and human genetic Databases; the need to address benefit sharing' (2006) 3 J* of International Biotechnology Law 89-103

[148] Knoppers, BM and Sheremeta, L "Beyond the Rhetoric: Population genetics and Benefit-sharing" (2003) 11 *Health L J* 89

[149] Brownsword, R "Genetic Databases: One for All and All for One?" (2007) 18 *King's Law Journal* 247-273

[150] Beyleveld D, "Data Protection and Genetics: Medical Research and the Public Good" (2007) 18 *King's Law Journal* 275-289

[151] 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 22

[152] 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; Haddow, G Laurie, G et al "Tackling community concerns about commercialization and genetic research: A modest interdisciplinary proposal' (2006) *Social Sciences & Medicine* (forthcoming)

outcomes. Public trust[153] will be an imperative for biobanks. Public trust is a fundamental cornerstone in genetic science and biobanking. Equally importantly, good research data should inform discussion on the development of biobanking.[154] Generally, the limited empirical research that has been undertaken indicates a cautious level of public confidence in favour of the development of databases for medical research. Empirical research[155] supporting this view of public support has been undertaken in Canada, Iceland,[156], Ireland,[157] Australia[158]and Sweden[159] Two projects in Britain have been especially concerned about public engagement. The funders of UK Biobank and the project's Ethics and Governance Council have commissioned public opinion surveys, while the set-up of the Generation Scotland project includes a specific branch dedicated to public engagement.[160] Biobanks must commit to their duties of good governance, probity, transparency and security[161]. There are a host of other unique questions raised by biobanks,

[153] 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 J Bovenberg "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.

[154] See Hirtzlin, I, et al, "An empirical survey on biobanking of human genetic material and data in six EU countries" (2003) 11 *European Journal of Human Genetics* (6) 475-488.

[155] See Caulfield, T and Outerbridge, T "DNA Databanks, Public Opinion and the Law" (2002) 25 *Clinical and Investigative Medicine* 252-256

[156] Caulfield, T "Perceptions of Risk and Human Genetic Databases: Consent and Confidentiality Policies" in G Armason et al (eds) *Blood and Data: Ethical, Legal and Social Aspects of Human Genetic Databases* University of Iceland Press and Centre for Ethics Reykjik 2002 at 283-289 and Kaiser, J "Population Databases Boom, From Iceland to the U.S" (2002) 298 *Science* 1158-1161

[157] Cousins, G et al "Public Perceptions of Biomedical Research: A Survey of the General Population in Ireland", Health Services Research Centre, World College of Surgeons in Ireland, Dublin 2005.

[158] See Williams "Australian Attitudes to DNA Sample Banks and Genetic Screening" (2005) 21 *Current Medical Research and Opinions* 1773-1775 and J Fleming "Issues with Tissues: Perspectives of Tissue Bank Donors and the Public Towards Biobanks and Related Genetic Research" in *Biobanks* Centre for Law and Genetics Symposium, September 2007.

[159] Kattis-Lindbland, A et al "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" (2007) 35

Scandanavian Journal of Public Health 148-156.

[160] See Generation Scotland website: http://129.215.140.49/gs/gpce.htm

[161] Other suggestions for the regulation of biobanks have included possible national registration. For example, the Australian Law Reform Commission *Essentially Yours: The Protection of Human Genetic Information in Australia* Report 96 2003. recommended that the registration of these

including autonomy and consent, public engagement, data-sharing, benefit-sharing, and international harmonisation There should be a renewed debate on ideas about the public good[162] with particular focus on compulsory participation, even a duty[163] to participate, in research for public health purposes and benefits. [164]Appropriate and effective regulation is a prerequisite to the development of the research potentialities of genetic research biobanks and, to a similar degree the development of the genomics industry. International harmonisation and consistency of biobank regulation on access to database information, transfer between countries, privacy regimes and policies are essential to realise the promise of biobank research.[165]

databases on the public register (Recs 18-1, 18-3). This would enable the NHMRC not only to track the genetic research undertaken in Australia but also ensure greater transparency and accountability for the biobanks. Registration would provide an effective and inexpensive audit trail in annual reports to the NHMRC.

[162] See, Beyleveld D, "Data Protection and Genetics: Medical Research and the Public Good" (2007) 18 *King's Law Journal* 275-289;Campbell, AV "The Ethical Challenges of Genetic Databases: Safeguarding Altruism and Trust" (2007) 18 *King's Law Journal* 227-245;Brownsword, R "Genetic Databases: One for All and All for One?" (2007) 18 *King's Law Journal* 247-273; and,; Caulfield, T "Biobanks and Blanket Consent: The Proper Place of the Public Good and Public Perception Rationales" (2007) 18 *King's Law Journal* 209-226

[163] Harris, J 'Research on Human Subjects', in Freeman, M and Lewis, A (Eds) *Law and Medicine*, Current Legal Issues Volume 3 OUP 2000 at 379-397.

[164] Brownsword, R "Genetic Databases: One for All and All for One?" (2007), *King's Law Journal*, 247-273.

[165] See comments Reymond, M et al "Ethical, Legal and Economical Issues Raised by the Use of Human Tissue in Postgenomic Research" (2002) 20 *Digestive Diseases: Clinical Reviews* 257-265.

Result of the Questionnaire on the Japanese Guidelines on Genomic/Genetic Research - with a proposal of amendments –

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Objectives of the Questionnaire 目的

Questionnaire on the Experiences and the Expectation of Researchers for the Reform of the Guidelines on Genomic/Genetic Research (Common Guidelines of Three Ministries)

Background
- Gap between the advancement of genomic/genetic research and the provisions of Guidelines
  The Guidelines cannot catch up the advancement ?
- Possibility of new developments (especially, Human Whole Genome Re-sequencing)
- To offer a basis for discussion for the reform of the Guidelines
- To aim at making a new guidelines for clinical use of genomic information

「ヒトゲノム・遺伝子解析研究に関する倫理指針(三省指針)改善のための研究者の経験と希望調査」

背景
- ヒトゲノム・遺伝子解析研究の進展状況と3省指針の乖離
- 今後の研究の新しい展開の可能性(特に全ゲノム再解析)

狙い
- 今後の指針改定作業の基礎資料
- 臨床研究から応用への橋渡しの模索

Questionnaire – Method アンケートの方法

- Questionnaire on 8 important issues in the Guidelines
  Ask researchers problems encountered in the experiences
  multiple choice + free written answer
  Aim at clarifying the current situation and the problems which researchers face in their research
  Try to avoid statistic data processing in order to clarify concrete situations
- Ask opinions on the Guidelines
  1. Necessity of matching the provisions of the Guidelines : On which points?
  2. Difficulties encountered in the research in the application of the Guidelines
  3. Examples of useful concepts / provisions
  4. Other opinions and suggestions

- 8つの重要問題についての経験調査
  多肢選択式＋自由記述式
  経験や問題点を事由に記述してもらうことによって、状況を明らかにしようとした
  （統計処理では捕捉しにくい具体的状況）
- 三省指針全体への意見
  1. 新時代への対応
  2. 研究上の困難
  3. 三省指針が役に立った例
  4. 三省指針に対する意見
  5. 他の参考法令、文書、ガイドライン（外国のものを含む）

Outline of the Answers 回答概要

Addressees : Researchers in genomic and genetic research in Japan (Names are picked up from different sources and covers leading researchers
Response : 212 / 942　22.2 %
Types of research
1) Multifactorial diseases (57.1)
2) Monogenic disorders (36.8)
3) Side effects (27.8)
4) Tracking research (21.7)
Insufficiency of the Guidelines (Q.4-1): 12.7
Difficulties in Informed Consent Procedure: 12.7
Disclosure of personal genetic information : 32.5 (from participant 91.3, family 37.7)
Difficulties in Ethical Review Procedure : 11.3
Difficulties in Joint research : 83.0 (with abroad 35.2)
Difficulties in Genetic Counseling : 25.5 (with apprticipant 85.2, blood relatives 64.8)
Issues relating to and necessity of provisions on Bank / Data base:
Protection of samples and genetic information 66.0,
Management and use 62.3,
Collection of samples 47.2

- 送付先　942
- 回答：212通　約20%の回答率
- 研究タイプ
  1）多因子疾患（57.1）、2）単一遺伝子疾患（36.8）
  3）副作用（27.8）、4）追跡型研究（21.7）
- 三省指針の対応不足、困難（問4-1）：12.7
- インフォームド・コンセントでの困難：12.7
- 遺伝情報の開示要求：32.5 （提供者91.3）家族（37.7）
- 倫理審査上の困難：11.3 （内容＝別紙参照）
- 共同研究：83.0 （海外35.2）
- 遺伝カウンセリングの希望：25.5 （提供者85.2、血縁者64.8）
- バンク・DBの必要措置：
  試料・データの保護66.0、管理運営62.3、サンプル収集47.2

Insufficiency of the Guidelines
指針の不十分さ

A. Limited scope of the Guidelines to research
⇒ Need of the guidelines for clinical use of genetic information
B. Insufficient response to "genetic business"
C. Excessively rigid provisions
= Need of attention to promote research
D. Coordination with other relevant guidelines
E. Insufficient response to pharmaco-genomics
F. Too narrow discretion of the researchers

A.研究と臨床との区別⇒医療への応用が困難
B.遺伝ビジネスへの対応
C.規定が厳格すぎる＝研究への配慮不足
D.他の指針との整合性
E.ファーマコゲノミクスへの対応
F.現場の裁量権の狭隘さ

Points for reform 改善するべき点

- Informed Consent Procedure
- Treatment of samples and data
- Joint research with foreign institutions
- Ethical review system
- New Types of research = biobank and database

- インフォームド・コンセント
- サンプルとデータの取り扱い
- 海外との共同研究
- 倫理審査制度
- 新しいタイプの研究
＝バイオバンク、DB