Human genetic research databases and biobanks: Towards uniform terminology and Australian best practice

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This article examines international best practice for the establishment, maintenance and use of human genetic research databases (HGRDs), particularly focusing on large-scale population biobanks, and considers the measures that should be taken in Australia to comply with this best practice. These HGRDs play a pivotal role in basic research aimed at understanding the basis of human disease at the genetic level, and applied research aimed at putting that basic knowledge into practical application. In particular, the large-scale biobanks are vital research tools in the drive to uncover the causes and consequences of human health and disease. Biobanks are being established at regional, national and international levels throughout the world. Although their governance structures are uniformly complex, some best practices are emerging with regard to consent (particularly consent to future research and withdrawal of consent), privacy and data protection and intellectual property, ownership and access. Best practices with regard to benefit-sharing are emerging much more slowly. This article reviews these international best practices with the aim of providing guidance for the development of appropriate regulatory structures in Australia.

INTRODUCTION

Collections of human tissue have been in existence for many years around the world. In addition to these existing collections, new small-scale and large-scale banks of human tissue samples and human genetic information continue to be established at ever increasing rates, prompted by advances in genetic analysis techniques. These collections of tissue and information provide the essential raw materials for many aspects of modern genomic research, and their value as research tools for wide-ranging research projects is increasingly recognised. All such collections that are capable of being used for research purposes are referred to collectively in this article as human genetic research databases (HGRDs). The OECD also uses this terminology to describe any collection of human genetic material intended to be used for research purposes.[1] Hence, the term "HGRD" is intended to be broad in scope, incorporating everything from collections of pathological samples through to databases of sequence information and large-scale biobanks that link genetic information derived from tissue samples with medical records and family histories.

All of the various forms of HGRDs are likely to continue to play a pivotal role in the ongoing endeavour to understand the basis of human disease at the genetic level, and to put that basic knowledge into practical application. DNA and RNA samples and sequence information, cell lines, tissues, cell preparations or plasma/blood samples are essential tools for pharmacogenomic research

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[1] 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) p 14.

and analysis that aims to identify potential biomarkers[2] or drug targets by any of the new generation genomic tests utilising DNA marker, RNA expression level or protein activity.[3] Human genetic research databases are also important resources for many other types of medical research that could benefit not only current patients but also future generations.[4]

Banking of human genetic material for research purposes, whether in the form of tissue samples or genetic information, raises a number of traditional, but also many novel, ethical, legal and social issues.[5] There are inevitable tensions in achieving the appropriate balance between facilitating access to HGRDs for research purposes, protecting participant autonomy and dignity, ensuring broader community benefit, facilitating commercial development and other matters. These tensions exemplify the need for appropriate laws, policies and research guidelines that balance facilitation and regulation of banking and access to banked materials.

The traditional ethical concerns of participant consent and the need to provide appropriate protection of privacy are always paramount in any biomedical research involving humans. But these issues are even more problematic for research related to HGRDs particularly, for the following reasons: first, the precise nature of consent requirements is unclear when tissue and information are stored for future unspecified research; and second, the protection of privacy is complicated when genetic information and medical and genealogical information have to remain linked for research purposes. Alongside these issues of consent to use for research purposes and protection of privacy, there are other equally valid and growing concerns about commercial ownership of HGRDs, direct commercial use of databanked material and the more indirect commercial use of the results of research that has utilised databanked material.[6] These concerns are closely linked to the consent question, because arguably fully informed consent requires disclosure of both direct and indirect commercial dealings with human genetic material and information. 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 is an essential precondition for the successful operation and future research benefit of HGRDs.[7]

The aim of this article is to examine international best practice for the establishment, maintenance and use of HGRDs and to consider the measures that should be taken in Australia to comply with this best practice. Some attention was given to this issue in the Australian context by the Australian Law Reform Commission (ALRC) and Australian Health Ethics Committee (AHEC) in their joint inquiry into the protection of genetic information, and a number of relevant recommendations were made in

[2] 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.

[3] See Shastry B, "Pharmacogenetics and the Concept of Individualized Medicine" (2006) 6 *Pharmacogenomics Journal* 16. The Generation Scotland project, which is run by a consortium of medical schools in Scotland with Scottish Executive funding, has this as an explicit objective: http://www.generationscotland.org viewed 11 December 2007.

[4] Kaiser J, "Biobanks: Population Databases Boom, from Iceland to the US" (2002) 298 *Science* 1158.

[5] Note that human genetic databanks can also have a variety of purposes outside the research context. The most obvious is databanking for forensic purposes. This article focuses exclusively on human genetic research databanks. For further information on forensic databanking see Chalmers D (ed), *Genetic Testing and the Criminal Law* (UCL Press, London, 2005). On legislation, see eg *Criminal Investigations (Blood Samples) Act 1995* (NZ) authorising New Zealand's national DNA databank. For a United Kingdom perspective see the report from the Nuffield Council on Bioethics, *The Forensic Use of Bioinformation: Ethical Issues* (September 2007), http://www.nuffieldbioethics.org/go/ourwork/bioinformationuse/publication_441.html viewed 12 December 2007.

[6] Nicol D, "Public Trust, Intellectual Property and Human Genetic Databanks: The Need to Take Benefit Sharing Seriously" (2006) 3 *Journal of International Biotechnology Law* 89; Stranger M, Chalmers D and Nicol D, "Capital, Trust and Consultation: Databanks and Regulation in Australia" (2005) 15 *Critical Public Health* 349.

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

Essentially Yours, the final report of the inquiry.[8] The recently revised *National Statement on Ethical Conduct in Human Research*[9] also has some relevant provisions, as does the *Privacy Act 1988* (Cth), as amended in 2006.[10] However, each of these documents lacks the specific guidance needed to ensure that all research using HGRDs in Australia complies with international best practice.

There is a palpable sense of urgency in discussions of this nature around the world. Appropriate mechanisms for regulating HGRDs have been considered in a number of countries and by a range of research or regulatory organisations.[11] In Australia the ALRC/AHEC inquiry[12] provided a valuable framework within which to consider these issues and the development of national guidelines more fully.

TERMINOLOGY

The term "biobank" is frequently used to describe large-scale collections of human tissue and genetic information specifically created for research purposes.[13] These large-scale collections generally also have other key attributes, which make them vital research tools in the drive to uncover the causes and consequences of human health and disease. One particular feature of these large-scale projects is that genetic information about an individual is often linked to other health information and genealogical information. It should be noted that the "biobank" terminology is not used consistently to describe all such projects.[14] For example, the Estonian Genome Project uses "genome database", the Latvian Genome Project uses "genebank" and the French National Ethics Consultative Committee uses "biolibraries".[15] This article uses the biobank terminology to describe all such projects hereafter.

A distinction needs to be drawn between biobanks and like collections mentioned above and other forms of HGRDs. The term "HGRD" incorporates both repositories of tissue and information that are created specifically for research purposes and also the many existing collections of human tissue that were created in the past primarily for diagnostic and clinical purposes, either without consideration of research or with research considered as a secondary purpose. The term "HGRD" also incorporates collections that were created for specific limited research purposes only, with specific and limited

[8] Australian Law Reform Commission, *Essentially Yours: The Protection of Human Genetic Information in Australia*, Report No 96 (Commonwealth of Australia, Canberra, 2003).

[9] National Health and Medical Research Council, Australian Research Council and Australian Vice-Chancellors' Committee, *National Statement on Ethical Conduct in Human Research* (Australian Government, Canberra, 2007) (the National Statement).

[10] *Privacy Legislation Amendment Act 2006* (Cth).

[11] The following examples are illustrative: Council of Europe, Steering Committee on Bioethics, *Draft Recommendations on Research on Biological Materials of Human Origin* (2005); Opinion of the European Group on Ethics in Science and New Technologies to the European Commission, *Ethical Aspects of Human Tissue Banking* (1998); Swedish Medical Research Council (MFR), *Research Ethics Guidelines for Using Biobanks, Especially Projects Involving Genome Research* (1999); Bioethics Advisory Committee of the Israel Academy of Sciences and Humanities, *Report on Population-based Large-scale Collections of DNA Samples and Databases of Genetic Information* (2002); Comité Consultatif National d'Éthique pour les Sciences de la Vie et de la Santé, *Ethical Issues Raised by Collections of Biological Materials and Associated Information Data; "Biobanks" and "Biolibraries"*, Opinion 77 (2003); ESRC Economic and Social Research Council, Research Ethics Framework, *Discussion Paper 2: The International Dimension to Research Ethics: The Significance of International and Other Non-UK Frameworks for UK Social Science* (2004); Working Group on DNA and Epidemiology (TUKIJA) of the Finnish National Advisory Board on Health Care Ethics (ETENE), *DNA Samples in Epidemiological Research* (2002); German National Ethics Council, *Biobanks for Research* (2004).

[12] ALRC, n 8, Recommendations 18-1 to 18-3 and 14-1 to 14-5. Dr Francis Collins, Head, United States National Human Genome Research Institute and Chair, Human Genome Project and HapMap Project, described the Report as "a truly phenomenal job, placing Australia ahead of what the rest of the world is doing" in a news release during the XIX International Congress of Genetics, Melbourne, 5-9 July 2003.

[13] Perhaps the best-known example is the United Kingdom Biobank Project, For further information, see http://www.ukbiobank.ac.uk viewed 11 December 2007.

[14] For further discussion of terminology, see Tutton R and Corrigan O, *Genetic Data Bases: Socio-ethical Issues in the Collection and Use of DNA* (London, 2004) pp 2-4. For further information on these large-scale collections, see Cardinal G and Deschênes M, "Surveying the Population Biobankers" in Knoppers BM (ed), *Populations and Genetics: Legal and Socio-Ethical Perspectives* (Koninklijke Brill NV, Netherlands, 2003).

[15] Comité Consultatif National d'Éthique pour les Sciences de la Vie et de la Santé, n 11.

consent regimes, as well as the broader-based biobanks established for use in multiple research projects. Despite these clear differences between biobanks and other types of HGRDs, the term "biobank" is often used interchangeably with the term "HGRD" to describe *any* collection of human tissue or human genetic information that can be used for research purposes. In this article, a clear distinction is maintained between the large-scale population biobanks and other types of HGRDs.

All HGRDs have the twin goals of facilitating genomic research and protecting of the welfare of the sample and information contributors.[16] But there are some particular ethical and legal issues that must be taken into account when considering the use of existing tissue collections and databases of genetic information for research purposes, particularly with regard to the consent requirement. The problem of consent to research use is likely to be of concern irrespective of whether such repositories were originally created for research or for other purposes. In contrast, biobanks are established with the specific aim of conducting research, with careful efforts to ensure that participant consent has been obtained. Before turning to these consent issues, it is necessary to explore more deeply the notion of biobanking.

ESTABLISHMENT AND GOVERNANCE OF LARGE-SCALE POPULATION BIOBANKS

Establishment of biobanks

Biobanks are being established at regional, national and international levels throughout the world.[17] For example, at the regional level, a number of biobanks have been or are in the process of being set up, including the following: the Karolinska Institutet (Sweden);[18] CARTaGENE (Quebec, Canada);[19] the Western Australian Genome Health Project;[20] the National Heart, Lung and Blood Institute (National Institutes of Health, United States);[21] and the Centre for Integrated Genomic Medical Research (Manchester, United Kingdom).[22] At the national level, the Icelandic Health Sector Database Project[23] was the pioneer program that was followed by a number of others, including GenomEUtwin (Finland);[24] Estonian Genome Project;[25] Danubian Biobank Consortium (involving six countries in Central Europe);[26] KORA-GEN (Germany);[27] LifeGen (Sweden);[28] INMEGEN (Mexico);[29] LifeLines (Netherlands);[30] United Kingdom Biobank;[31] and Generation Scotland.[32] These regional and national biobanks have been specifically created for large-scale longitudinal genetic research projects.

[16] See National Bioethics Advisory Commission Report, *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance*, Vols 1 and II (Bethesda, Maryland, 1999), http://govinfo.library.unt.edu/nbac/pubs.html viewed 11 December 2007. See also National Bioethics Advisory Commission Report, *Ethical and Policy Issues in Research Involving Human Participants*, Vols 1 and II (Bethesda, Maryland, 2001), http://govinfo.library.unt.edu/nbac/pubs.html viewed 11 December 2007.

[17] See Cardinal and Deschênes, n 14. Also see 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" (2004) 8 *TRAMES* 15 at 15.

[18] See http://ki.se/ki/jsp/polopoly.jsp?d=866&a=1306&l=en viewed 11 December 2007.

[19] See http://www.cartagene.qc.ca/accueil/index.asp?l=e viewed 11 December 2007.

[20] See http://www.genepi.org.au/waghp viewed 11 December 2007.

[21] See http://www.nhlbi.nih.gov viewed 11 December 2007.

[22] See http://www.medicine.manchester.ac.uk/cigmr viewed 11 December 2007.

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

[24] See http://www.genomeutwin.org viewed 11 December 2007.

[25] See http://www.geenivaramu.ee/index.php?lang=eng&show=main viewed 11 December 2007.

[26] See http://www.danubianbiobank.de/DanubPublic/misc/mscHome.jsp viewed 11 December 2007.

[27] See http://www.gsf.de/epi/en/netw_KORAGEN1.html viewed 11 December 2007.

[28] See http://www.lifegen.de/index.php4 viewed 11 December 2007.

[29] See http://www.inmegen.gob.mx/index.php?lang=es viewed 11 December 2007.

[30] See http://www.lifelines.nl/index.php viewed 11 December 2007.

[31] See http://www.ukbiobank.ac.uk viewed 11 December 2007.

At the international level, the successor to the Human Genome Project, the International Haplotype Mapping Project (the HapMap Project) is a collaboration between the United States, the United Kingdom, Japan, Nigeria, China and Canada which aims to identify and compare genetic similarities and differences in collected human tissue samples to find genes that affect health, disease and medication responses.[33] The Public Population Project in Genomics (P3G)[34] 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

Governance of biobanks

Governance is a major topic of international debates associated with biobanking. To date, the governance structures for these new large-scale population biobanks are uniformly complex. Indeed, it has been said that they can be "staggeringly expensive"[35] to establish and operate. Establishment involves negotiations with health officials, researchers, governing institution(s), research funding agencies, health consumer/community organisations and ethics experts. Some of the biobanks mentioned above have been established by national legislation providing for governance by a private company[36] or an independent foundation.[37] The vehicle of a charitable trust has also been recommended as an appropriate governance entity.[38]

Given the particular ethical issues associated with large-scale banking of tissue and its linkage with genetic, medical and genealogical information, a number of biobanks have established independent ethics bodies charged with oversight of the establishment, maintenance and use of the biobank.[39] For example, the United Kingdom Biobank has an independent Ethics and Governance Council (EGC) to monitor and advise on the Biobank's operations. In some countries, there is a requirement for the oversight body to report to the relevant government minister.[40] Apart from considerations of structure, one of the tasks of a biobank's governing body is to introduce guidelines for the ethical operation of the biobank,[41] together with standard operating procedures.[42]

[32] See http://www.generationscotland.org viewed 11 December 2007.

[33] See http://www.hapmap.org viewed 11 December 2007.

[34] See http://www.p3gconsortium.org viewed 11 December 2007. The P3G motto is "transparency and collaboration".

[35] Greely H, quoted in Longtin R, "Canadian Province Seeks Control of Its Genes" (2004) 96 *Journal National Cancer Institute* 1567.

[36] For example, the *Health Sector Database Act 1998* (Iceland) provides for the granting of an exclusive licence to deCODE Genetics to manage the database. However, the Icelandic Supreme Court (judgment No 151/2003, 27 November 2003) suggested that this legislation was 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".

[37] For example, the *Human Genes Research Act 2000* (Estonia) provides for ownership and control of the Estonian genome database by the Estonian Genome Project Foundation. See also *Biobanks in Medical Care Act 2002* (Sweden).

[38] Winickoff D and Winickoff R, "The Charitable Trust as a Model for Genomic Biobanks" (2003) 349 NEJM 1180. However, such a model is not problem-free: see Boggio A, "Charitable Trusts and Human Research Genetic Databases: The Way Forward?" (2005) 1-2 *Genomics, Society and Policy* 41 and a further response: Winickoff DE and Neumann LB, "Towards a Social Contract for Genomics: Property and the Public in the 'Biotrust' Model" (2005) 1-3 *Genomics, Society and Policy* 8.

[39] See United Kingdom Biobank, *Ethics and Governance Framework, Version 2.0* (2006), http://www.ukbiobank.ac.uk/ethics/egf.php viewed 11 December 2007. Similarly, it is planned that CARTaGENE will have an independent Institute for Population, Ethics and Governance: see http://www.p3gconsortium.org/cartagene.cfm viewed 11 December 2007.

[40] Generation Scotland also includes a Generation Scotland Advisory Board with an oversight function: see http://129.215.140.49/gs/GSAB.htm viewed 11 December 2007.

[41] See eg National Cancer Institute, *Best Practices for Biospecimen Resources* (June 2007), http://biospecimens.cancer.gov/practices viewed 11 December 2007.

[42] See eg OECD Working Party on Biotechnology, *Draft Guidelines for Human Genetic Research Databases* DSTI/STP/Bio (Paris, 2007); Trouet C, "New European Guidelines for the Use of Stored Human Biological Materials in Biomedical Research" (2003) 30 *Journal of Medical Ethics* 99.

Public trust in biobank research is widely acknowledged as an essential aspect of biobank governance.[43] It is well recognised that the governance arrangements for biobanks should include procedures that allow public scrutiny and encourage public trust.[44] Indeed, public engagement has been a major feature of the development of the major public biobanks.[45] For example, the EGC of the United Kingdom Biobank holds public meetings on its activities and publishes the minutes of all of its deliberations.[46]

Another important aspect of biobank governance that is likely to promote public trust is for the control of the biobank samples and data to be vested in a body or individual independent of the researchers seeking access to data or samples. This idea of trusteeship has been described in the Ethics and Governance Framework of the United Kingdom Biobank as acting "as the *steward* of the resource, maintaining and building it for the public good in accordance with its purpose" (emphasis added).[47] In Australia, the ALRC/AHEC Report gave some support to the idea that an independent body should be responsible for biobank governance.[48]

There are a number of technical requirements that must also be met to ensure effective, secure and ethical biobanking, many of which are also applicable to other forms of HGRDs.[49] Most importantly, because health data and genetic information are particularly sensitive personal information, this information should be protected by encryption codes and only be accessible to properly authorised biobank employees and researchers under strict conditions.[50] Computing systems must not only be efficient and reliable, they must secure confidentiality and privacy of the information derived from the samples. 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 particularly for authenticating and checking information.

Biobank laboratories and collection and testing facilities are generally required to comply with prescribed national accreditation standards.[51] In particular, sample collection and storage processes must be quality assured to ensure that the collection, handling, storage, processing, access and use of any samples are not tainted by human or processing error. In addition, there are technical issues associated with the number of data points that must be collected in relation to each individual sample and 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

[43] Campbell, n 7; Hansson M, "Building on Relationships of Trust in Biobank Research" (2005) 31 J Med Ethics 415.

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

[45] See OECD, *Creation and Governance of Human Genetic Research Databases* (2007) particularly Ch 3.5, "Public Engagement in the Establishment of a Population Database".

[46] See http://www.egcukbiobank.org.uk/meetingsandreports/index.html viewed 11 December 2007.

[47] See http://www.ukbiobank.ac.uk/ethics/egf.php viewed 11 December 2007. See also the "custodian" proposal by the Irish Law Reform Commission, *The Establishment of a DNA Database*, Report 78 (2005) Ch 4.

[48] The ALRC and AHEC in their inquiry into the protection of genetic information recommended that best practice in genetic research involving genetic databases requires 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. See ALRC, n 8, Recommendation 16-1.

[49] National Cancer Institute, n 41; 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* 5.

[50] 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 NEJM 2527.

[51] Increasingly, national accreditation standards align with international standards developed by bodies such as the International Organisation for Standardisation (ISO). For example, see New Zealand, Ministry of Economic Development, *Review of New Zealand's Standards and Conformance Infrastructure* (Wellington, NZ, September 2005) p 36: "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."

degree of interchangeability of data between biobanks wishing to conduct international research projects.[52] The industry itself is in the process of developing its own standards through biobank networks to answer concerns about inconsistencies in the collection, storage and access policies of biobanks.[53]

CONSENT PROCEDURES

Core consent obligations

The issue of participant consent to enrolment in an HGRD is, and has been, one of the most debated and vexed ethical questions.[54] The collection of all human tissue samples must be carried out in accordance with legal and accepted ethical standards, particularly the informed consent of the sample donor. This need for fully informed consent is particularly well recognised with regard to tissue deposits in large-scale population biobanks. Consistent with established international standards for research generally, consent procedures for biobanking purposes must respect participant autonomy[55] by providing detailed and explicit information to participants, opportunities for further explanation of, and time to understand, the information. Accordingly, proper consent to involvement in biobanking should include participant information, understanding and voluntary consent to a whole range of factors, which might include the following:[56]

- the relevant risks and benefits, if any;
- the types of samples and data to be collected and stored;
- the possibility that the research to be undertaken may disclose information about related family members. Consent should be explicitly sought as to whether or not this can be communicated (see below);
- the nature and scope of the intended research to be undertaken. Consent to future unspecified research needs to be addressed explicitly (see below);
- the possibility that there may be sharing of samples and data with other research organisations;
- the procedures by which researchers access data/samples;
- the collection of other data from health-relevant or genealogical records;
- the procedures for later re-contact, where necessary;
- the arrangements for the protection of privacy, security and confidentiality, including restrictions on the release of information to insurers and employers;
- anonymisation procedures and restrictions on re-identification;
- the procedures for feedback of research results and how they will be reported;
- the right to withdraw;
- the arrangements relating to the participant's data/samples in the event of incapacity or death;
- the biobank's policy on benefit-sharing;
- the prospect for intellectual property to be created and the potential commercial involvement; and
- the absence of any personal financial gain for any participant.[57]

[52] See OECD, n 45, particularly Chs 3 and 4 on Privacy and Confidentiality.

[53] For example, in Australia and New Zealand, the voluntary, not-for-profit Australasian Biospecimen Network is developing standardisation advice: http://www.abrn.net viewed 11 December 2007.

[54] See eg Campbell, n 7 at 239-243.

[55] 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* 209; and Campbell, n 7.

[56] See eg OECD, n 42, Principles 5A-5H, Best Practices 5.1-5.9 and Annotation para 27.

[57] Similarly, the Human Genome Organisation Ethics Committee, *Statement on Human Genomic Databases* (December 2002) declares that human genomic databases are a public resource (1(b)); all humans should share in and have access to the benefits of databases (1(c)); and individuals should have choices with regard to donation, storage and use of samples and the information derived therefrom (4(a)). The Statement goes on to declare that participants should be informed of the degree of identifiability of their data (4(c)) and the possibility that samples or the information derived therefrom might be shared with other researchers, including those in other countries or commercial entities (4(d)). See http://www.hugo-international.org/Statement_on_Human_Genomic_Databases.htm viewed 11 December 2007

The consent processes for biobanking (and more generally, for all HGRDs) must, at their heart, emphasise the following core requirements:

- the voluntary nature of the consent;
- the right to obtain one's own information; and
- the right to withdraw from the database.

But biobanking goes beyond mere compliance with the legal formalities of the original consent requirements, raising wider issues of the public interest and public good. Academic commentary is increasingly calling for a change in focus to recognise other human rights beyond the principle of autonomy, particularly the principle of human dignity, which has been argued to underpin human rights provisions in national Constitutions and international Conventions.[58]

Consent to future research

Biobanks are established with the express aim of conducting *long-term* research where human tissue that is collected and the data that are derived from it will be stored and used for future research. Whether samples and data can be used for future research projects depends on the nature and scope of participant consent. There may be three distinct levels:[59]

- limited/specific consent for research use for a specific project;
- qualified/follow-up consent where a participant wishes to be contacted in the future if there is to be any extension of or substantial variation from the original research project; or
- full/unspecified consent enabling use for multiple research purposes, both present and future.

The first level of specific consent is usual in medical research generally. Such a narrow form of consent would not usually be sought for biobanking purposes, since one of the key rationales of large-scale population biobanks is that the whole resource should be available for future research purposes. At the second level, the participant consents to a specific project and consents to be re-contacted in the future. This type of consent is also referred to as "re-consent". It may arise in circumstances where it is necessary either to collect new information or samples for an existing research project, or to seek consent for new research uses not within the existing consent. In either case, the original participant consent would have to be reviewed by an Ethics Review Board (ERB). The ERB must be satisfied that, after proper consideration of the information provided to the participant and the nature of the original consent, the participant has given permission to the researchers to obtain re-consent.

The third level of full/unspecified consent, sometimes referred to as "broad"[60] or "blanket" consent, is the most useful from the biobank's perspective. Here the biobank has consent for one or more approved research projects and also for the use of the tissue/data for future research that has not yet been through the ethics review process. This type of consent is not common in health research and is the subject of continuing debate and some controversy.[61] For a valid broad/unspecified consent, there must be specific mention in the original participant consent that tissue/data collected and stored *for one purpose* may be used for *other* future and unspecified research.

In all cases, participant consents must be reviewed on an ongoing and routine basis to ensure that collection, use, storage and release of the tissue and/or information are consistent with the actual consent given. Indeed, it has been suggested that the long-term commitment that participants make to biobanks necessitates some form of follow up (re-check) and periodic re-consent to ensure that the

[58] Beyleveld D and Brownsword R, *Human Dignity in Human Ethics and Bio-law* (OUP, Oxford, 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.

[59] These levels of consent are specified in general research ethics guidelines (see eg the Australian National Statement, n 9) and in specific biobank guidelines (see eg the United Kingdom Biobank, n 39, pp 9-10).

[60] Hansson M, "Should Donors Be Allowed to Give Broad Consent to Future Biobank Research?" (2006) 7 *The Lancet Oncology* 266.

[61] Caulfield, n 55.

intention, understandings and voluntariness of the original consent continue.[62] Furthermore, each individual research project must be fully scrutinised by an appropriately constituted ERB.

Withdrawal of consent

International ethical research standards require that participants should be free at any time to withdraw consent and to withdraw from further involvement in the project. In the case of 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 and may involve withdrawal of consent, samples and data at different levels, depending on the consent and choice of the participant. Three levels of withdrawal can be identified:

- *no further contact*: here the participant expresses the wish not to be contacted again directly, but consents to retention and use of previously provided data/samples, and permission may also be given to obtain health-relevant records;
- *no further access*: at this level, the participant allows retention and use by the biobank of the data/sample but does not consent to any further contact and gives no permission to obtain health-relevant records; or
- *no further use*: under this option, there is no further contact with the participant, and samples and health-related information must be destroyed (but not data already used).[63]

Disclosure of health-related information

Research using materials stored in HGRDs has the potential to reveal medically relevant information about the health or future health of participants and possibly, their offspring or relations. It is essential that clear policies are established on whether such information will be disclosed to the participants and what procedures are to be followed for disclosure. The question of whether or not to disclose is particularly problematic for the large-scale biobanks simply because of the scale of the research endeavour. Nevertheless, it has been argued that there is an ethical obligation to disclose, and, in the case of the United Kingdom and other European Union countries, there may in fact be not only an ethical duty but also a legal duty through Art 2 of the *European Convention on Human Rights*.[64] Whichever policy option may ultimately be chosen, it should be clearly communicated in writing to the participant at the recruitment stage. The participant should be informed about whether health-relevant information will or will not be disclosed to the participant, the participant's offspring or relations. One important consideration is whether a qualified genetic counsellor should disclose the information or whether such a counsellor should be available to explain the significance of the results.

Consent procedures for previously collected samples

It has been commonplace for hospitals and specialist clinics to retain collections of human tissue[65] since the 19th century, when preservation techniques were first introduced.[66] In 1998 in the United States, the former National Bioethics Advisory Committee (NBAC) estimated that there were more than 282,000,000 specimens stored in that country alone and further estimated that the accumulation rate from blood tests, surgery and other medical procedures was probably in the region of 20,000,000 specimens per year.[67] The report noted that the types of existing collections of human tissues range

[62] 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, London, 2004).

[63] This three-tiered structure is used by the United Kingdom Biobank: see n 39.

[64] 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.

[65] See United Kingdom Medical Research Council, *Policy and Guidance on Human Tissue*, http://www.mrc.ac.uk/PolicyGuidance/EthicsAndGovernance/UseofHumanTissue/index.htm viewed 11 December 2007.

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

[67] National Bioethics Advisory Commission, *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance* (Maryland, 1999) Vol I, pp 13-15. See comments in Knoppers B, "DNA Banking: A Retrospective-Prospective" in Burley J and Harris J (eds), *A Companion to Genethics* (Blackwell Publishing, Oxford, 2002) p 379.

from pathology samples collected for clinical/diagnostic purposes through to newborn screening cards and umbilical cord blood banks. To this list should be added specialised human tissue collections, particularly of cancer tissue, used for specialist research.[68]

These collections of tissue and data held in long-term storage are generally not covered by patient consent. However, such tissue collections provide valuable sources of material for use in research. In the past, it was frequently the case that pathology samples collected for routine diagnostic and clinical purposes were also used for research purposes. Hospitals and other institutions holding tissue did not presume refusal, or implied refusal, of consent by patients but rather presumed 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".[69]

The distinction between these *existing* collections of human tissue and *future* collections is significant from both the ethical and legal perspectives. Generally, most countries allow stored tissue to be used in research provided that the project is scientifically assessed and approved by an ERB and that the samples are properly de-identified.[70] Effectively, in such circumstances the ERB waives the requirement for express consent.[71] Waiver of consent is not uncommon in epidemiological research and human tissue research. Generally, national codes of research ethics specify a number of factors that must be given due consideration by ERBs in deciding whether or not to waive consent. De-identification of samples or information is generally recognised to be of major importance.

National codes of research ethics generally distinguish between *identified, de-identified* and *re-identifiable* information. The UNESCO *International Declaration on Human Genetic Data* (2003) adopts similar distinctions, providing the following definitions:

- *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;
- *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; and
- *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. However, use of these terms is not consistent and may pose difficulties for developing an international framework.[72]

It is unfortunate that the terminology used is not consistent as this may pose difficulties that must be resolved in determining international best practice.[73] However, in Australia there are now three settled categories of data description, which determine best practice at the national level.[74]

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

[69] For this quote and further helpful discussion on this point see the Singapore Bioethics Advisory Committee Report, *Human Tissue Research* (2002) at [9.1]-[9.6], http://www.bioethics-singapore.org viewed 11 December 2007. Note the use of the term "legacy tissue" to describe existing collections.

[70] Singapore Bioethics Advisory Committee Report, n 69 at [9.1]-[9.6].

[71] In Australia, see Zeps N et al, "Waiver of Individual Patient Consent in Research: When do Potential Benefits to the Community Outweigh Private Rights?" (2007) 186 MJA 88.

[72] See Knoppers BM and Saginur M, "The Babel of Genetic Data Terminology" (2005) 23 *Nature Biotechnology* 925; 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* 661; Knoppers BM et al, "Genomic Databases and International Collaboration" (2007) 18 *King's Law Journal* 291.

[73] Knoppers and Saginur, n 72.

[74] In Australia, the newly revised National Statement refers to individually identifiable, re-identifiable and non-identifiable data: see n 9, Ch 3.8, "Databanks".

PRIVACY AND DATA PROTECTION

Privacy/data protection legislation

Privacy of personal information is an accepted legal and ethical principle and privacy law now has a major influence on the regulation of medical research generally and HGRDs in particular. The operators of all HGRDs 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 HGRD. Privacy legislation is fairly standard in most countries because of the original OECD privacy principles developed in the early 1980s.[75] In Europe, members of the European Union (EU) are required to implement legislation compliant with the EU *Data Protection Directive* (95/46/EC).[76] The two major North American nations also have complex data protection regulation arising from their federal arrangements.[77] Some Asian countries have also introduced data protection by legislation.[78]

Privacy legislation has established a range of principles from collection through to the storage and use of data. The Australian National Privacy Principles[79] are summarised below, but similar principles are found in most jurisdictions.

- 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).
- 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 any record about them and details about the nature and purposes of the record.
- Principle 6: Persons should have access to records about them, unless restricted by law.
- Principle 7: Record-keepers should 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 should check that personal information is accurate and up-to-date before use.
- Principle 9: A record-keeper cannot use personal information except for relevant purposes.
- Principle 10: A record-keeper should not to use personal information unless the person consents; use is authorised by law; there is reasonable belief of a threat to life or health; it is for law enforcement; or use is directly related to the purpose for which the information was collected.
- Principle 11: A record-keeper should not disclose personal information unless the person is aware that the information is likely to be passed on; the person consents; disclosure is authorised by law;

[75] For example, in Australian the governing legislation is the *Privacy Act 1988* (Cth).

[76] *Act Concerning the Protection of Privacy with Regard to the Treatment of Personal Data Files 1992* (Belgium) updated 1998; *Personal Data Protection Act 1996* (Estonia); *Personal Data Act 1999* (Finland): *Data Protection Act 1978* (France) amended by *Data Protection Act 2004*; *Data Protection Act* or *Bundesdatenschutzgesetz 1997* (Germany) amended in 2002; *Act on the Protection of Individuals with Regard to the Processing of Personal Data 2000* (Iceland); *Data Protection Act 1998* (Ireland); *Data Protection Act 1999* (Spain); *Personal Data Act* or *Personuppgiftslagen 1998* (Sweden); *Federal Data Protection Act 1992* (Switzerland); *Data Protection Act 1998* (UK).

[77] The *Privacy Act 1985* (Can) regulates the federal public sector. The *Personal Information Protection and Electronic Documents Act 2000* (Can) applies to private sector commercial activities throughout the country. In the United States the *Privacy Act 1974* (US) protects records of United States government agencies

[78] See eg the *Computer-Processed Personal Data Protection Law 1995* (Taiwan).

[79] See *Privacy Act 1988* (Cth), s 14.

there is reasonable belief of a threat to life or health; it is 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.

Privacy legislation generally includes a right of access to and correction of personal information (see Principles 6 and 7 above). In addition to these general access rights in privacy legislation, some countries (and States within federal systems) have supplemented their privacy laws with specific statutory rights to patients, particularly in relation to access to medical records.[80] There can also be court-authorised access to personal information where access is refused for improper reasons.

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 and approved by a Privacy Commissioner or Ombudsman.[81] Generally, complaints do not go to court but are dealt with administratively by the Privacy Commissioner or Ombudsman.

In addition to this privacy/data protection legislation, contract law can also play an important role in protecting privacy and confidentiality. Employees of HGRD operators are usually bound by codes of ethics, incorporated as terms of their contracts of employment. Similarly, researchers using HGRDs are usually bound by ethical and legal duties of confidentiality in material transfer agreements (MTAs)[82] or in research access agreements. These duties require employees and researchers to maintain confidentiality of information acquired in the course of their work relating to the operation of the HGRD or use of the HGRD resource for research purposes. Breaches of duties of confidentiality can lead to dismissal from employment. For biobanks established by legislation, the governing Act usually includes a statutory offence for unauthorised disclosure of information.[83]

Research guidelines

"Hard law" privacy/data protection 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. It establishes the four key pillars for ethical review by properly constituted ERBs in medical research:

- voluntary consent of the research participant;
- independent review of the project;
- assessment of the risk; and
- involvement of competent researchers of integrity and research merit.

These guidelines are contained in national codes of ethical conduct in research in most countries.[84] The trend in most countries is towards greater regulation of human research and away from earlier

[80] United States: protections for medical records are found in the *Health Insurance Portability and Accountability Act 1996* (US). In April 2003, Standards for Privacy of Individually Identifiable Health Information were introduced; Finland: *Act on the Status and Rights of Patients 1993* and *Medical Research Act 1999*; Sweden: the health and medical sector is regulated by *Health Care Register Act 1998* and *Patients' Records Act 1985*.

[81] Finland: Data Protection Ombudsman; France: Commission Nationale de l'Informatique et des Libertes; Spain: Data Protection Agency (Agencia Espanola de Proteccion de Datos); Sweden: Data Inspection Board (Datainspektionen); Canada; Privacy Commissioner of Canada; New Zealand: Office of the Privacy Commissioner; United Kingdom: Office of the Information Commissioner; United States: there is no independent privacy oversight agency in the United States.

[82] The following draft clause has been formulated by the United States National Cancer Institute: "The Recipient will in no way attempt to identify or contact the person(s) from whom the MATERIAL was collected or derived. Under no circumstances will the key to coded samples be given to the Recipient under this Agreement." See National Cancer Institute, n 41, cl 9, App 2.

[83] For example, see s 128 of the *Human Genes Research Act 2001* (Estonia).

[84] See eg the Australian National Statement, n 9.

self-regulation.[85] Importantly, the approval processes by ERBs must ensure that appropriate procedures are in place "to protect the privacy of subjects and to maintain the confidentiality of data".[86]

In addition to these national codes, most of the large-scale population biobanks have special ethics and governance oversight frameworks that have been introduced in legislation or in guidelines and policies. These frameworks provide specific guidance on best practice with regard to the protection of privacy.[87] The OECD has recommended that it is best practice to establish such oversight bodies.[88] Similarly, in the United States, the Department of Health and Human Services, the National Institutes of Health and the National Cancer Institute[89] have jointly developed a comprehensive template set of guidelines, policies and procedures for HGRDs supporting such oversight.[90]

ACCESS, OWNERSHIP AND INTELLECTUAL PROPERTY

As HGRDs have a primary public research focus, access for research purposes should be facilitated to the greatest extent possible, bearing in mind the need for appropriate regulation to protect participant privacy and related matters. This public research focus does not preclude private companies from applying, subject to conditions, to use HGRD data and resources. The pharmaceutical industry is particularly interested in the use of large-scale population biobank resources for pharmacogenomic research, in the hope that this may herald a new generation of medicines tailored to individual needs. This research may enable better patient stratification, if not individualised medicine, thus achieving better patient outcomes from the drug administration perspective.

The problem with commercial involvement, however, is that it may arouse some public anxiety and distrust.[91] In Australia, eg, the ALRC/AHEC public consultation process uncovered public scepticism about the continuing "heavy degree of commercialisation of [medical and genetic] research" and concerns that participant altruism could "lead to billion dollar profits for multinational pharmaceutical companies".[92] Recognising that commercialisation challenges public trust in science,[93] a policy of transparency and public engagement by biobanks and other HGRDs in relation to their commercial activities is advisable. With this in mind, the Generation Scotland project is carrying out an ongoing program of public engagement, focusing especially on issues and concerns about commercialisation.[94]

As noted at the start of this article, it is important to distinguish between commercial ownership of HGRDs, direct commercial use of databanked material and the more indirect commercial use of the results of research that has utilised databanked material.

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[85] Chalmers D, "Research Involving Humans: A Time for Change?" (2004) 32 *Journal of Law, Medicine and Ethics* 583.

[86] This is the United States Common Rule formulation, as found in the 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, n 69; and the Japanese *Guidelines for the Protection of Personal Information in Businesses that Use Human Genetic Information* (2004).

[87] For a good example of this approach, see the Singapore Bioethics Advisory Committee Report, *Personal Information in Biomedical Research* (2007), http://www.bioethics-singapore.org viewed 12 December 2007.

[88] See OECD Working Party on Biotechnology, n 42, Principle 3B, Best Practice 3.1-5.9 and Annotations paras 18, 19.

[89] National Cancer Institute, n 41; International Society for Biological and Environmental Repositories, "Best Practices for Repositories I: Collection, Storage, and Retrieval of Human Biological Materials for Research" (2005) 3 *Cell Preservation Technology* 1 at 5-48, http://www.isber.org/Pubs/BestPractices.pdf viewed 11 December 2007.

[90] 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 Graeme Laurie).

[91] Nationaler Ethikraat, *Opinion on Biobanks for Research* (Berlin, 2004) p 27.

[92] 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) p 19.

[93] Chalmers and Nicol, n 7.

[94] See Generation Scotland website at http://129.215.140.49/gs/gpce.htm viewed 11 December 2007; also see Haddow G, Laurie G et al, "Tackling Community Concerns about Commercialization and Genetic Research: A Modest Interdisciplinary Proposal" (2007) 64 *Social Sciences & Medicine* 272.

Ownership of HGRDs and HGRD resources

The question of ownership of body parts and tissue remains unsettled in both common and civil law jurisdictions.[95] In general, the large-scale population biobanks try to clarify this issue by informing participants that they are not entitled to ownership of samples or information held by the biobank. The United Kingdom Biobank, eg, states that participants "will have no property rights in the samples"[96] and that this will be explained in the consent process. Similarly, the Estonian Genome Project states that ownership of samples vests in the Project. This does not preclude the capacity of sample donors to have agreed rights to access to information or to withdraw from the project, or, in some cases, to have the sample destroyed. To avoid confusion, consent documents should also clarify that the sample donor does not have and will not obtain any share in or control over intellectual property rights in the database, in research results or in any product arising from the research use of the biobank.

In addition to ownership or "stewardship"[97] of the collection of tissue samples and other tangible components of the HGRD, intellectual property rights might also exist in the HGRD itself (as opposed to intellectual property in research that utilises HGRD resources). For example, database protection may be available. 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 in recognition of the work and costs in compiling, verifying and presenting data. The governing foundations of some biobanks (eg, Iceland, Estonia and the United Kingdom) establish that the intellectual property accruing from the creation and development of the database vests in the biobank.

Access to HGRD resources and ownership of the results of research utilising HGRD resources

For many small-scale HGRDs, the operator of the HGRD will also be the researcher utilising the resource. In such situations, issues of access to the resource and ownership of research results, as between the HGRD and the researcher, are a non-issue. However, access and ownership arrangements are likely to be far more complex for large-scale population biobanks and other HGRDs that are made available to other researchers. A study commissioned by the National Cancer Institute National Dialogue on Cancer provides an insight into how ownership and access issues are dealt with by HGRDs focusing on cancer research in the United States.[98] The final report discusses best practice in a range of areas. With regard to access, it makes the following recommendations:

- use should only be for the purpose specified in the application for access;
- no attempt should be made to obtain identifying information;
- there should be no transfer to third parties without prior written permission of the HGRD; and
- any publication resulting from use of the materials should acknowledge the HGRD.

These requirements appear to be in compliance with obligations to provide a basic level of protection to HGRD participants. On the issue of ownership of research results, it was found in the study that, as a matter of practice, most HGRDs did not retain any rights to downstream intellectual property produced using the material they distribute, unless they undertook collaborative research, in which case the intellectual property may be jointly owned.[99] As a general rule, the institution or organisation where the research was conducted claimed ownership of the intellectual property rights. The final report further concluded that, where databanked materials are made available to researchers, it is best practice to require an MTA to be executed in accordance with the same terms as the best

[95] For a discussion of property and donor samples see Bovenberg, n 7 (2004).

[96] United Kingdom Biobank, n 39, Section A, "Stewardship of Data and Samples", p 14.

[97] Using the language adopted by the United Kingdom Biobank, n 39.

[98] Eiseman E, Bloom G, Brower J, Clancy N and Olmsted SS, *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 (Rand Science and Technology, Arlington VA, 2003), http://www.rand.org/pubs/monographs/MG120 viewed 11 December 2007.

[99] Eiseman et al, n 98, p 138.

practice intellectual property policy. This is important, because it gives contractual force to the terms of the intellectual property policy included in the MTA. While disputes about contribution and ownership will inevitably arise, it is probably fair to say that, as a general rule, where intellectual property and access policies of this nature are in place, they are likely to provide an acceptable level of clarity for the relevant parties (HGRD operators, researchers and downstream commercial developers).

An early draft of the United Kingdom Biobank *Policy on Intellectual Property and Access* was cast in somewhat similar terms in that it had the usual provision that intellectual property arising out of research using the resource would vest in the investigator creating it.[100] However, the access policy was somewhat unusual in that it provided that, as a general rule, researchers would not be provided with access to stored tissue. Instead, the draft policy provided that analysis would be undertaken by the Biobank or a laboratory contracted by it. The policy further provided that an access agreement would have to be entered into, and an access fee would need to be paid, although fees for non-commercial research were intended to be nominal. Where tissue was provided, a standard form MTA would need to be executed. Access policies and MTAs of this nature do have the advantage of allowing operators of biobanks to retain vital control over the material to which they provide access. However, time will tell whether this policy is ultimately implemented by United Kingdom Biobank, and whether it can actually work in practice. The draft policy is no longer available on the United Kingdom Biobank website, and hence its current status is uncertain. In any case, it seems unlikely that an access regime of this nature could be employed more generally by biobanks that lack the type of financial and infrastructure support provided to United Kingdom Biobank by the Wellcome Trust and the United Kingdom Medical Research Council.

Once intellectual property has been created and the more indirect commercial use of the results of research that has utilised HGRD resources has commenced, it is unlikely that HGRDs will be able to retain much control over the commercialisation process. However, intellectual property and access policies may impose obligations on the commercial partner to share the benefits arising from commercial exploitation of research utilising HGRD resources. This important issue is discussed below.

Participant and community concerns about access and ownership

Community concerns with commercialisation of research must be tackled by demonstrating the public benefits that may flow from this research.[101] As a general accepted ethical principle, the results of research should normally be published and disseminated to contribute to the advancement of public knowledge.[102] Some of the large-scale information databases have policies to this effect, requiring release the entirety of information held in the database into the public domain. For example, the HapMap Project[103] and GenBank[104] both follow this policy.

In general, all HGRDs should commit to the principles of publication and dissemination, requiring research to be published in the scientific literature or in other ways in a timely fashion, to allow assessment and scrutiny of the results. Ideally, raw data should also be shared to the greatest extent possible.[105] However, where research is undertaken by, or in partnership with, a private organisation, eg by a pharmaceutical company, there may be policies or restrictions on publication and

[100] Copy on file with the authors.

[101] Haddow et al, n 94.

[102] See eg the Australian National Statement, n 9, s 1.3(d): "disseminating and communicating, whether favourable or unfavourable, in ways which permit scrutiny and contribute to public knowledge".

[103] See http://www.hapmap.org viewed 11 December 2007.

[104] See http://www.ncbi.nlm.nih.gov/Genbank viewed 11 December 2007.

[105] This statement is not intended to trivialise the complexities associated with data sharing and exchange. On this point see Milanovic F, Pontille D and Cambon-Thomsen A, "Biobanking and Data Sharing: A Plurality of Exchange Regimes" (2007) 3 *Genomics, Society and Policy* 17.

dissemination of results to protect the commercial value of the results.[106] In such situations, non-disclosure should be kept to a minimum and publication should occur as soon as the necessary period of confidentiality has expired.

Potential conflicts of interest must be audited and managed in collaborations and partnerships between commercial organisations and HGRDs. The general principle of disclosure of interest is recognised in national codes for the responsible conduct of research.[107] There are also well-established policies of science and medical research journals requiring declarations of financial associations with commercial organisations before, and as a condition of, publication. Transparency is the key.

BENEFIT-SHARING

Many commentators refer to a "crisis" in public trust in biomedical research.[108] One aspect of the public trust problem is that private companies are perceived as making huge profits from the exploitation of intellectual property developed using tissue and information that has been freely donated. This problem is likely to be exacerbated in relation to HGRDs if the operators of the HGRDs and the researchers using the databanked materials and information become involved in the commercialisation processes.[109]

There is no doubt that commercialisation is increasing, both at the storage and the research phases, even where these are conducted in publicly funded institutions. The usual justification for this is that industry involvement is necessary to boost public funding and to ensure that research results are actually translated into new developments in health care. In return, the industry partner secures ownership of intellectual property arising from the research. This all seems to make good sense in theory: researchers get to do their research, investment by industry is protected and the public interest is served because new health care products are developed. However, one problem with this is that participants who voluntarily provide their tissue and information "seem to be left out of the loop and it is not difficult to see why they may feel somewhat marginalised, and even exploited".[110]

Why, then, do people continue to participate in this type of research? It is widely recognised that people generally participate for purely altruistic reasons, because of the likely benefit that such research brings to society as a whole. They may also have other personal reasons for participating, eg if they or their families suffer from a particular medical condition which they believe may be alleviated as a result of the research. Although some research participants are paid for their participation (eg, in some clinical trials), as a general rule payment is rarely considered to be a serious option, because of long-standing concerns about the commodification of human tissue. In the increasingly commercialised research environment, where everyone but the research participant appears to have a financial interest, the altruistic model of participation is under serious threat.

While some would argue that the solution is to pay participants a fair price for use their material,[111] this view is not widely supported. On the contrary, in addition to the potential for this to impact on the cost of doing biomedical research, there is concern that it could lead to coercion to participate.[112] In the alternative, benefit-sharing is being mooted both as an ethically appropriate means of balancing the conflicting interests involved in genetic databanking and also as potential solution to the problem of loss of public trust.

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[106] See generally, Chalmers and Nicol, n 7.

[107] See, as an example, *Australian Code for the Responsible Conduct of Research* (2007).

[108] See eg Stranger, Chalmers and Nicol, n 6; Petersen A, "Biobanks' 'Engagements': Engendering Trust or Engineering Consent?" (2007) 3 *Genomics, Society and Policy* 31.

[109] See Nicol, n 6 at 92.

[110] See Nicol, n 6 at 92.

[111] Bear JC, "'What's My DNA Worth Anyway?' A Response to the Commercialization of Individuals' DNA" (2004) 47 *Perspectives in Biology and Medicine* 273.

[112] For example, Andrews L and Nelkin D, "Homo Economicus: Commercialization of Body Tissue in the Age of Biotechnology" (1998) 28 *Hastings Center Report* 30.

The need to address benefit-sharing in human genetic databanking has been discussed for some time in the academic literature and at the international policy level. In particular, it has found expression in guidelines prepared by UNESCO[113] and the Human Genome Organisation.[114] 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.[115] It has been argued that the rhetoric of this principle should be replaced with the implementation of appropriate and practical mechanisms for benefit-sharing.[116]

Despite these arguments in favour of benefit-sharing, the incorporation of such considerations into actual HGRD policies has been slow, although some models are emerging.[117] For example, a report by the Newfoundland and Labrador Department of Health and Community Services has recommended that benefit-sharing arrangements should be required for *any* human genetic research with commercial potential and that the provincial government should play a central role in negotiating suitable arrangements.[118]

It is unlikely that there will be one single model for benefit-sharing in all circumstances. But now is the time for all parties engaged in databanking to seriously consider how to implement appropriate benefit-sharing arrangements. They should not see benefit-sharing as a threat to the commercial success of the endeavour but as an important component in its success. Discussions of this nature are particularly important in relation to large-scale population biobanks simply because of their scale and the challenges they bring to traditional notions of altruism, individualism and autonomy.[119]

CONCLUSION

In harmony with similar developments in genomic research around the world, HGRDs are being established with regularity in Australia. Although there is no intention to date to create a national biobank along the lines of the United Kingdom Biobank and like projects in other jurisdictions, there are some examples of larger-scale projects.[120] In particular, at the regional level, the Western Australian Institute of Medical Research is playing a lead role in the consolidation of HGRD resources in that State.[121] The National Health and Medical Research Council (NHMRC) is supporting the Western Australia project together with a number of other facilities. These biobanks promise both an increase in the capacity for genomic research and an improvement in research quality in this country.

As previously noted in this article, the final report of the joint ALRC/AHEC inquiry into the protection of genetic information[122] recognised the significant privacy and ethical issues posed by

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

[114] HUGO, *Statement on Benefit Sharing 2000*.

[115] 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 *Journal of Law, Medicine and Ethics* 7; Nicol, n 6.

[116] Knoppers BM and Sheremeta L, "Beyond the Rhetoric: Population Genetics and Benefit-sharing" (2003) 11 *Health Law Journal* 89.

[117] See generally Nicol, n 6.

[118] Newfoundland and Labrador Department of Health and Community Services, *Policy Implications of Commercial Genetic Research in Newfoundland and Labrador* (2003) p 12, http://www.nlcahr.mun.ca/research/reports_search/DP_Final__Report.pdf viewed 11 December 2007. See also Haddow et al, n 94.

[119] See generally Glasner P, Atkinson P and Greenslade H, *New Genetics, New Social Formations* (Routledge, London, 2006).

[120] Examples include the Australian Motor Neurone Disease DNA Bank; Genetic Repositories Australia; National Leukemia and Lymphoma Tissue Bank; Australian Rheumatology Association Database; Australian Childhood Diabetes DNA Repository.

[121] See Western Australian Government Office of Population Health Genomics, *e-newsletter* (April 2007), http://www.genomics.health.wa.gov.au/news/docs/e-newsletter_Apr07.pdf viewed 11 December 2007.

[122] See n 8.

HGRDs and recommended that they should be regulated. Building on these recommendations, a new chapter was inserted into the revised National Statement in 2007.[123] The NHMRC is now in the process of developing more detailed guidelines for the governance of biobanks. In this regard, significant guidance can and should be drawn from the international developments discussed above, not only to ensure conformity with international best practice but also to assist Australian researchers in establishing collaborative relationships internationally that accord with the highest ethical standards.

Public trust[124] will be an imperative for the development of Australian guidelines on good governance, probity, transparency and security for all HGRDs.[125] Biobanking and other HGRD activities also raise a host of related questions about consent, public engagement, data-sharing, benefit-sharing and international harmonisation. Some of these are unique and others are variations on traditional themes. Biobanking and other forms of databanking may also renew debates on ideas about the public good,[126] with particular focus on participation, even a duty to participate,[127] in research for public health purposes and benefits.[128] The research potential of all HGRDs, and particularly the large-scale biobanks, will only be fully realised if appropriate and adequate regulatory structures are in place.

[123] See n 9, Ch 3.

[124] On the broad issue of public trust in biomedical research see Chalmers and Nicol, n 7; Bovenberg, n 7 (2005); Bovenberg, n 7 (2004).

[125] One other suggestion that has been mooted for the regulation of biobanks is a system of national registration. For example, the ALRC/AHEC final report, n 8, recommended registration of HGRDs on the public register (Recommendations 18-1, 18-3). This would enable the NHMRC not only to track genetic research being undertaken in Australia but also to ensure greater transparency and accountability for HGRDs. Registration would provide an effective and inexpensive audit trail in annual reports to the NHMRC.

[126] See Beyleveld D, "Data Protection and Genetics: Medical Research and the Public Good" (2007) 18 *King's Law Journal* 275; Campbell, n 7; Brownsword R, "Genetic Databases: One for All and All for One?" (2007) 18 *King's Law Journal* 247; and Caulfield, n 55.

[127] Harris J, "Research on Human Subjects" in Freeman M and Lewis A (eds), *Law and Medicine, Current Legal Issues* (OUP, Oxford, 2000) Vol 3, pp 379-397.

[128] Brownsword, n 126.