Human Research Tissue Banks / Resources / Biobanks Guiding Principles

1 Introduction

1.1 This paper contains guiding principles applicable to the management and operation of a human biosample resource / bank in the ethical and legal environment of the UK from 2006 onwards. These are the guiding principles that underpin the National Cancer Research Institute's (NCRI) Confederation of Cancer Biobanks (CCB).

1.2 Organisations providing any of the services of procurement / acquisition, annotation / quality control, storage, cataloguing and distribution of human biological samples use various terms to describe themselves. These include bank, biobank, resource, repository, collection, archive, library and others. Many of these organisations use a variety of terms to describe the nature of the human biological samples that they obtain and provide. These include tissue, biosample and biospecimen, often with additional reference to a particular disease (e.g. cancer bank), a specific body organ or tissue (e.g. brain bank, blood bank), an extract of the primary sample type (e.g. DNA bank), etc. Acquisition of samples may be primarily with the intent of research use or may follow use for clinical diagnostic or treatment purposes.

1.3 The guiding principles in this document can be applied to all such organisations, irrespective of the terms applied; below, they will be referred to generically as biobank(s) and biosample(s). The term biosample should be taken to include accompanying clinical data, without which it has no utility.

1.4 The guiding principles contained in this paper are derived from a variety of sources. In particular they reflect the views of several leaders of national not-for-profit human research biobanks from a number of countries, as represented by the Marble Arch Working Group [1]. These views are also in keeping with opinions expressed in other publications and other forums, both national and international, in recent years. The CCB wishes to promote these principles to build broad consensus within the biobanking and medical research community. These guiding principles are intended to be consistent with the *UK Funders' Vision for Human Tissue Resources* published in September 2011.

[1] Riegman, P. H. J.; Morente, M. M.; Betsou, F.; De Blasio, P.; Geary, P.; Marble Arch International Working Group on Biobanking for Biomedical Research (2008). "Biobanking for better healthcare". *Molecular Oncology* **2** (3): 213–222.

1.5 Biobanks are not isolated entities. They exist within an "ecosystem" of stakeholders that is diverse and includes the public, patients, healthcare workers, scientists, government, funders of science, providers of healthcare services, ethicists, regulators and others. Biobanks play a central role in a multidisciplinary **chain of supply** that extends from donors through to researchers, influenced by the many stakeholders who interact with the supply processes. Each person or organisation interacting with this chain of supply has a responsibility to adhere to over-arching guiding principles, to ensure that biosample supply is served and benefits realised.

1.6 The guiding principles proposed here place responsibility on all involved to maintain **chains of trust, custodianship and benefit** along the supply chain for biosamples from donors to researchers. In addition, such activities should be conducted with **appropriate consent** (see below and 5) and under **cost-contribution financial models** for the provision of biosamples for clinical research.

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1.7 Appropriate consent should be generic and enduring. Use of samples for defined studies, with specific consent for each study, does not constitute biobanking in accordance with these guiding principles, since samples cannot be made available to other researchers or for further studies without additional consent. The biobanking and research use of samples obtained primarily for clinical purposes, for which consent may not have been sought from patients, is governed by specific requirements of the Human Tissue Act, 2004 in England, Wales and Northern Ireland.

2 Biosample resources are for the public benefit

2.1 This is the principle of **maintaining the chain of benefit.**

2.2 Human research biosamples only exist as a consequence of donation by members of the public, who may be patients or healthy donors. Donations of samples are typically altruistic and specifically intended to further research into human health and disease.

2.3 Where biobanks are funded in whole or in part by public or charitable funds, the funds are also given to be used for the wide public good.

2.4 Therefore, individuals or organisations in receipt of such samples or funds should be mindful of their responsibilities and moral obligations to act within an ethical framework, and with integrity. They should use these samples, or make them available to others for use, in the best interests of the public and not solely in the interests of themselves or their organisations.

2.5 Any researchers who are capable of conducting studies to produce public benefit are valid end-users of samples. This includes researchers in publicly or charitably funded institutions and those in commercial organisations (e.g. pharmaceutical or biotechnology companies). Biobanks should operate policies and procedures to ensure that *bona fide* researchers in any of these sectors can be granted access to their collections.

2.6 Access to biosamples should, wherever possible, be provided on the basis of the likelihood of the samples being put to a good and beneficial use in a timely fashion after donation.

2.7 Individuals or organisations that are end-users of samples should only request access to biosamples they intend to use. Samples should only be supplied by a biobank on a "defined-use" basis, to allow samples to remain available for use by others towards further potential benefit.

2.8 Where samples are collected for a specific study, a single person or institution may be generating a collection, acting as custodian, and also be the first end-user of the samples. During the period of such a study, it is legitimate to restrict access to the samples to the principal investigator and named collaborators. Once the initial study has been completed, such collections should, wherever possible, be opened up for wider research. At this stage the collection takes on the characteristics of a biobank as defined in this document and these guiding principles should be taken to apply.

2.9 End-users should rarely, if ever, be asked to return samples to a biobank as, outwith the custody of the bank, it may be impossible to ensure the continuing fidelity of the samples and subsequently guarantee their quality and suitability for use by others.

2.10 Biobanks should ensure that adequate means are in place to review the competence of applicants as well as the adequacy and appropriateness of the science and ethics of applications for biosamples prior to supply to end-users. These review processes should ensure respect of the conditions of donor consent and the donors' intentions to generate benefit. Biobanks should facilitate access by mechanisms that maintain the chains of trust, custody and

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supply for benefit. Application and review processes should not be constructed with intrinsic conditions that deter or hinder access to samples.

2.11 Circumstances may exist in which biosamples are reserved to prevent their depletion and allow their use in a more significant study at a future time-point.

2.11.1 It may be necessary to operate different access policies for different sets of samples depending on circumstances (e.g. a precious set of biosamples representing a very rare condition might be accessible on different terms from samples affected by a common disease).

2.11.2 It is not possible to predict all such circumstances or the necessary policies. However, restriction of access should be transparent and only be practised in rare, well defined, circumstances to avoid excluding more near-term uses and benefits arising from the donations.

2.11.3 Those involved in biosample banking should produce appropriate policies balancing duties to restrict access to some rare or precious samples against the general responsibility to make samples readily available wherever possible. Access should only be restricted as an exception.

2.12 Biosamples, prior to research use, represent latent information / data stores that will be deciphered through the research conducted on them. Once this information is realised, the principle of benefit would suggest that these data should also be available for sharing with others to maintain the chain of benefit in a fashion analogous to the sharing of the samples themselves.

2.12.1 Individuals along the chain of supply, and their employing organisations should subscribe to the principle of sharing data, as should the funders of research. Mechanisms or data-sharing policies should be in place for this to occur. A number of NCRI partners have such policies applying to the research they fund. Biobanks should adhere to these policies as appropriate, and promote the principle of data-sharing at all times.

2.12.2 It will be necessary to create circumstances in which this can occur while also accommodating the need for researchers to protect professional interests such as their right to first publication and / or rights to protect intellectual property or commercial / competitive advantage resulting from their research.

3 Biobanks should protect public trust

3.1 This is the principle of maintaining the **chain of trust**.

3.2 Biosamples for research are donated on a basis of trust. Loss of public trust jeopardises research biobanking and all of its potential benefits. Even a minor event associated with adverse publicity can have very significant, widely felt and long-lasting detrimental effects on legitimate biobanking.

3.3 Those involved in the supply chain downstream of the donor have a responsibility to protect that trust.

3.4 Individuals or organisations acting as biobanks should operate a culture of open communication, transparency, fairness and accountability to all stakeholders, but particularly donors and the public, to maintain trust.

3.5 Any individuals or organisations who pervert the supply chain or the chain of benefit in the interests of themselves or of their organisation, however well intended, risk betraying donors' trust.

3.6 Legal agreements (e.g. contracts or material transfer agreements) between parties who exchange biosamples for research should include provisions to maintain the chains of trust and benefit and to respect the provisions of the original donor consent along the full extent of the supply chain.

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4 The operators of biobanks are custodians of the biosamples therein

4.1 This is the principle of maintaining the **chain of custody**.

4.2 Human research biobanks participate in supply chains in which biosamples pass between parties, originating from the donor and ultimately being used in research studies.

4.3 By ethical and legal convention there are no ownership rights over a part of the human body once that part has been removed from a donor. Anyone who is in possession of a part of a body acts as a **custodian** of the tissue and derived biosamples. They have a responsibility to the original donor, in compliance with the consent applying to the donation, to fulfil the donor's intentions as far as possible.

4.3.1 An exception to this may apply if the biosample has been materially altered by someone who has applied skill to create a product derived but modified from its native state (e.g. an immortalised or genetically modified cell line). Further work is required to clarify when such an exception might apply in the context of research biobanking.

4.3.2 This is a claim that can be made regarding some processed derivatives of biosamples and is the basis on which these samples are sometimes openly sold as products for profit.

4.3.3 The distinction between a native (but stabilised or preserved) biosample in a biobank and a processed or manufactured product derived from a biosample is ill defined at present and open to dispute. Further work to clarify this boundary is required. (see also 9 below)

4.4 All participants in the supply chain should act responsibly as custodians to maintain the chain of supply, the chain of trust and the potential chain of benefit. Custodians should not assume rights of ownership as these will almost inevitably interfere with the purpose of the gift intended by the donors.

4.5 Possession or custodianship of biosamples, or enrichment of the utility of samples through processing or annotation, should not be used unreasonably to claim intellectual property rights. Neither individual samples nor large cohorts of samples represent a scientific discovery or invention. Their use may only contribute in part to the overall portfolio of work required to claim intellectual property in such a discovery or invention.

4.5.1 Donors should be asked, at the time of consent, to waive any financial interest in intellectual property that might arise from use of their sample(s).

4.5.2 Biobanks should recognise that they do not have intellectual property rights to encourage use of the resources and accommodate inventiveness by end-user researchers in the interests of fostering the originally intended benefits.

4.5.3 Recipients of biosamples from biobanks, and their employing institutions should be required to manage actively any intellectual property generated from their use of the samples, to ensure that discoveries made can be translated into greatest benefit.

4.5.4 Since IP rights cannot be claimed by biobanks there are no restrictions to biobanks honouring or acknowledging contributors, or prevent them from requiring end-users to acknowledge the contributions of the biobank, its funders and donors.

4.6 Where property rights can be claimed as a result of the application of skill, as in 4.3.1 above, the creators of these biosamples derivatives still have moral responsibilities to the original donors to maintain the chains of trust and benefit by sharing of these products under reasonable terms, to allow supply to other users.

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4.7 Difficulties may arise when organisational changes occur in relation to a biobank, such as a change of management personnel, merger of parent organisations such as NHS Trusts, policy change by funding bodies, closure of a study management group, etc. Disputes have arisen, for example, when researchers have relocated a sample collection to another institution when changing jobs. In the past, provision for such circumstances has been haphazard and governance requirements often poorly defined. Individuals or organisations acting as custodians should have plans for maintaining continuity in such circumstances; in effect, an "ethical preservation order" should exist to protect biobanked samples for the long term.

5 Biosamples should be obtained by donation with appropriate consent

5.1 Biosample donation for use in biomedical research should be made in the context of informed consent. As well as details of any specific studies planned for samples, it is important that the process of obtaining generic research consent includes information or discussion about the range of potential uses to which samples may be put, in particular where these may be sensitive or emotive to the donor.

5.2 Acquisition, storage and use of samples for research without consent are acceptable only in circumstances in which consent is deemed legally and ethically unnecessary within the prevailing regulatory environment. Agreement is required on the circumstances in which such a waiver might apply.

5.3 Consent means different things in different cultures and jurisdictions. Further work is required to understand potential donors' views / concerns and implement acceptable practices for gaining consent in various circumstances,

5.4 Policies for UK recognition of the consent to donate provided in cultures / jurisdictions that are substantially different from the regulatory environments pertaining in the UK (or other research-active countries) need to be developed, and vice versa. This is necessary to realise the benefits of research studies that can only be achieved by international collaboration.

5.5 Equally, it can be beneficial (and is often desirable) for biobanks to supply samples to research teams outside the country where the samples have been collected and stored. This is particularly the case when expertise to conduct a study exists overseas or when biosample numbers available within a single country are not sufficient to address a research question. To avoid ambiguity and operate a culture of openness, donors should be made aware that biosamples may leave the country where originally collected.

6 Biobanks are integral to the provision of healthcare, although often secondary to the primary healthcare of the donors

6.1 Most biosamples are collected from donors in healthcare settings during the course of diagnostic or therapeutic interventions in the direct interests of the donors as patients.

6.2 When samples are taken for healthcare reasons, it is imperative that the immediate and foreseeable clinical interests of the donor are served as the first priority. These may include retaining surplus material that might reasonably be required for future clinical use, which will be a matter for informed clinical judgement in individual cases. The principle remains that it is good practice to seek consent to use such residual material for research and that, as far as possible, patients' wishes to contribute to research in this way are respected.

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6.3 Research into human health and the development of new interventions against disease are important components of healthcare delivery. Therefore, providers of healthcare should see research biobanking as a valid activity that is not at odds with their primary clinical aims.

6.4 It is possible, in many circumstances, to accommodate the provision of direct healthcare and also to facilitate research biobanking. Where appropriate, efforts should be made to cater for sample donation in a healthcare setting as a routine and positive component of providing healthcare to patients.

7 Biobanks exist to provide a quality service

7.1 Quality management should be integral to the operational management of any biobank.

7.2 An individual or organisation who does not attend to quality management of the individual biosamples (comprising both biological material and accompanying clinical data) and overall collection diminishes the utility of the Biobank, disrupting the chains of trust and benefit.

7.3 Commitment to provide a service is necessary in the management of a biobank.

7.4 An individual or organisation providing a poor service to donors and/or researchers diminishes the utility of the resource and disrupts the chains of trust and benefit.

7.5 Biosamples are best held in specifically designated facilities and premises to maintain quality and security and ensure integrity of the chains of trust, benefit and supply.

8 Human biobanks should be purposeful

8.1 Wherever possible, the collection, storage and distribution of human biosamples for research should be driven by real scientific needs.

8.2 The creation of stockpiles of biosamples for no currently anticipated use has limited scientific merit and should not be the operating standard for most biobanks unless there is very strong justification. The latter may be the case, for example, for samples from donors with rare diseases, collection of which over many years in the absence of defined uses may be necessary to accrue a valid research resource.

8.3 Those who manage biobanks should not be passive participants in the supply chain, but should work to lead opinion and promote the merits of research using the biosmples and data they hold. This is essential to maintain the chains of trust and benefit.

9 Biosamples should not be traded as commodities

9.1 Human biosamples cannot be owned per se and therefore cannot be assigned a monetary value.

9.2 Processes involved in creating, maintaining and providing the services of biobanks cost money and it is legitimate for those operating biobanks to levy administrative fees when supplying samples to others.

9.3 Fees may be levied in two circumstances:

9.3.1 To recover contributions towards the costs (direct and indirect) incurred by the individuals or organisations operating the resource.

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9.3.2 In exchange for services that add utility to the biosamples (to be distinguished from "added value" which, by definition, is not a concept applicable to biosamples that have no intrinsic monetary value). It may be legitimate to generate a profit from the skill and endeavour employed to provide these "added-utility" services.

9.4 Further debate is required to define boundaries between the types of work undertaken within a biobank that can only justifiably be charged for to recover costs and work which may be deemed as adding utility.

9.5 Fees associated with the supply of biosamples should be related to the actual costs of work required to acquire, store and supply those samples. They should not be determined by other market forces such as rarity or supply-and-demand imbalance that assign value to samples artificially.

10 Summary

10.1 It is widely believed that the early decades of this century will see intense activity in the field of human biosample research worldwide and hence there is a need to promote best practice in biobanking. There is a window of opportunity to achieve high standards and performance in the biobanking community to maximise the contributions of carefully and ethically collected biosamples to the advancement of human biology and medicine.

10.2 It is also considered by experts in the field that human research biobanking needs to mature rapidly in terms of ethics, governance, policies and practices. This is essential to protect the interests of the donors and avoid losing public trust (and future donations) due to any further adverse publicity arising from misunderstood or inappropriate collection of human tissue.

10.3 Biobanking is a multidisciplinary endeavour that involves diverse stakeholders along a supply chain. It is essential that the spirit, purpose and benefit of the activity are not lost along the chain. Commonly agreed guiding principles are required, based on the need to maintain interlinked chains of trust, benefit and custody along the supply chain, respecting the need for donor engagement and consent and avoiding any treatment of human biosamples as a commodity.

10.4 Such guiding principles for the ethical and legal operation of human research biobanks are natural accompaniments of an informed and proportionate regulatory environment.

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