

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 The organisations providing any of the services of procurement / acquisition, annotation / quality control, storage, cataloguing and distribution of human biological samples use various terminologies to describe themselves. These include bank, biobank, resource, repository, collection, archive, library and others. Similarly, 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, biospecimen, a specific disease term (e.g. cancer bank), a specific part of the body (e.g. brain bank, blood bank), an extract of the primary sample type (e.g. DNA bank), etc. The guiding principles in this paper can be applied to all such organisations irrespective of the terms applied.
- 1.3 The guiding principles contained in this paper are derived from a variety of sources. In particular, they reflect a composite of the views of several leaders of national not-for-profit human research biobanks from a number of countries, as represented by the group known as the Marble Arch Working Group. These views are also in keeping with opinions expressed in other publications and in other fora, both national and international, in recent years. However, to date there is no published consensus statement containing these principles from any group other than the NCRI CCB. The CCB wishes to promulgate these principles to build broad consensus within the wider community beyond the membership of the CCB.
- 1.4 Biobanks / biosample resources, etc are not isolated entities. They exist in an “ecosystem” or community 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 the *multidisciplinary “chain of supply”* that extends from the donors through to the end-user researchers under the influence of the many stakeholders who interact with the supply chain. Each person or organisation interacting with the supply chain has a responsibility to adhere to common overall guiding principles and ensure that biosample supply is served and benefits realised.
- 1.5 The guiding principles proposed can be summed up by the responsibilities on all involved to maintain the **chains of trust, custodianship and benefit** along the supply chain for samples from donors to end-user researchers. In addition, such activities should be conducted with **consent** and under **cost-contribution financial models** for the onward provision of samples along the supply chain.

2. Biosample resources are for the public benefit

- 2.1 This may be summed up as the principle of maintaining the **“chain of benefit”**.
- 2.2 Human research biosample resources only exist as a consequence of **sharing** - the altruistic act of donation by members of the public, who may be patients in a healthcare setting or healthy donors in other settings. These donations of samples are intended to further research into human health and disease.

- 2.3 Where biosample resources are funded in whole or in part by public or charitable funds, again these are levied or gifted to be used for the wide public good.
- 2.4 Therefore, individuals or organisations in receipt of such samples (or funding) should be mindful of the responsibilities and moral obligations to act within an ethical framework and with integrity to use these samples and / or make them available to others for use in the best interests of the public and not solely in the interests of themselves, their organisation or their own research interests.
- 2.5 Any researchers who are capable of conducting studies to derive public benefit are valid end users of samples. This includes researchers in publicly or charitably funded institutions as well as those in commercial organisations (e.g. a pharmaceutical or biotechnology company). Biobanks should derive policies and procedures to ensure that bona fide researchers in any of these sectors can be granted access to resources.
- 2.6 Access to samples 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 samples 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. End users should rarely, if ever, be asked to return samples to a biobank as, outwith the custody of the biobank, it may be impossible to ensure the continuing fidelity of the samples and subsequently warrant their quality and suitability for use by others.
- 2.8 Biobanks should ensure that adequate means are in place for reviewing the competence of applicants as well as the adequacy and appropriateness of the science and ethics of applications for access to resources prior to supply of samples to end-users. These processes of review should take account of the responsibilities to respect the conditions of donor consent, and the intentions of the donors to generate benefit. Biobanks should facilitate access by mechanisms that maintain the chains of supply, trust, custody and benefit. Application and review processes should not be fundamentally constructed to deter or hinder access to samples.
- 2.9 Circumstances exist where samples may need to be reserved to prevent depletion of the resource and allow them to be used in a more significant study at some point in the future.
 - 2.9.1 It may be necessary to operate different access policies for different sets of samples available in different circumstances (e.g. a precious set of samples of a very rare condition might be accessible on different terms from samples of a common disease).
 - 2.9.2 It is not possible to predict all such circumstances and predict the policies necessary here. Recognition of such circumstances is difficult and restriction of access should only be practised in rare and well defined circumstances to avoid restricting more near-term uses and benefits arising from the donations.
 - 2.9.3 Those involved in biosample banking should produce appropriate policies that balance the duties to reserve access to some rarer or precious samples against the general responsibility to make samples readily available wherever possible and to only restrict access as an exception.
- 2.10 Samples prior to use in research metaphorically represent latent information / data stores that will be deciphered through the research conducted on the samples. Once this information is derived from the sample through research, the principle of benefit would suggest that this **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.

- 2.10.1 Individuals and organisations along the chain of supply should subscribe to the sharing of data and mechanisms / data-sharing policies should be in place for this to occur. A number of NCRI partners have such policies which apply to the research they fund. Biobanks should adhere to these policies as appropriate, and promulgate the principle of data-sharing at all times. (For example, the Medical Research Council Statement on Data Sharing and Preservation Policy 2005 and the Wellcome Trust's "Fort Lauderdale Agreement" 2003).
- 2.10.2 It will be necessary to create circumstances in which this can occur whilst also accommodating of the need for researchers to protect professional interests such as right to first publication or right to protect intellectual property or commercial / competitive advantage resulting from their research efforts.

3. Biosample resources should be based in donation with consent

- 3.1 Biosample donation for use in biomedical research should be given in the context of informed *consent as the gold standard*.
- 3.2 Acquisition, storage and use of samples for research without consent are acceptable, but only in circumstances in which consent is deemed legally and ethically unnecessary. Agreement is required on when such waivers of the need for consent might apply.
- 3.3 Consent means different things in different cultures and jurisdictions and further work is required to find acceptable common principles and practices for gaining consent in various circumstances.
- 3.4 Policies for reciprocal recognition of the consent to donation provided in one culture / jurisdiction that is very different from the means of gaining consent in the UK (or any other research active country) need to be developed. This is necessary to allow the benefits of research studies that can only be achieved on an international basis to be realised.
- 3.5 Equally, it can be beneficial, and is often desirable, for biobanks to supply samples to research teams outside of the country where the samples were collected and stored. This is particularly the case where the expertise to conduct a study exists overseas or where sample numbers within a single country are not sufficient to address a research question. For the avoidance of doubt and to operate a culture of openness, donors should be made aware that samples may leave the country of origin.

4 Biosample resources should protect public trust

- 4.1 This may be summed up as the principle of maintaining the *"chain of trust"*.
- 4.2 Samples are donated on a basis of trust. Loss of public trust jeopardises research biobanking and the potential benefits it may bring. One small "scandal" can have very significant and widely felt detrimental effects on legitimate biosample banking.
- 4.3 Those involved in the supply chain downstream of the donor have a responsibility to protect that trust.
- 4.4 Individuals or organisations acting as biosample resources should operate a culture of communication, transparency, fairness and accountability to all stakeholders, but particularly donors and the public, to maintain trust.
- 4.5 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 the trust of the donors.

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

5. Biosample resources are integral to the provision of healthcare, although often secondary to the primary healthcare of the donors

- 5.1 Most samples are collected from donors in healthcare settings and in the course of diagnostic or therapeutic interventions in the direct interests of the donors as patients.
- 5.2 It is imperative that the interests of the donor are served in preference to the interests of research biobanking in these circumstances, for example by using the samples for diagnostic purposes.
- 5.3 However, research into human health and the development of new interventions against disease are valid components of the delivery of healthcare. Therefore, providers of healthcare should see research biobanking as a valid activity and one that is not at odds with their mission.
- 5.4 It is possible in many circumstances to accommodate both 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 act of providing healthcare to patients.

6. The operators of biosample resources act as custodians

- 6.1 This may be summed up as the principle of maintaining the “*chain of custody*”.
- 6.2 Human research biosample resources participate in supply chains where the samples pass between parties originating from the donor and ultimately being consumed through research.
- 6.3 Supply chains have often been disrupted in the past by disputes over issues such as ownership, custodianship and access rights. (see also 2.9)
- 6.4 By ethical and legal convention there are no ownership rights over a part of the human body once that part has been removed from the donor. Anyone who is in possession of a part of a body acts as a *custodian* of the sample and has a responsibility to the original donor, under the terms of the consent applying to the donation, to fulfil the intentions of the donor as far as possible.
- 6.4.1 An exception to this is where the part of the body has been materially altered by someone who has applied skill resulting in a product derived from, but modified from, the native state. Further work is required to clarify when this is applicable in the context of research tissue banking.
- 6.4.2 This is a claim that can perhaps be made regarding processed derivatives of samples and is the basis on which these samples are sometimes openly sold as products and for profit.
- 6.4.3 The line between a native (but stabilised or preserved) sample in a bank and a processed or manufactured product derived from a sample is ill-defined at present and open to dispute. Further work to clarify this boundary is required. (see also 9 below)

- 6.5 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 or possession as these will almost inevitably interfere with the purpose of the gift by the donors.
- 6.6 Possession or custodianship of samples, or enrichment of the utility of samples through processing or annotation, should not be used to unreasonably confer intellectual property rights. Neither Individual samples nor large cohorts of samples represent a scientific discovery or invention. Their use may only contribute partially to the overall portfolio of work required to claim intellectual property in such a discovery or invention.
- 6.6.1 Therefore, donors should be asked to waive continuing financial intellectual property interests in their sample at the time of consent.
- 6.6.2 In turn, biobanks should also waive intellectual property rights to encourage use of the resources and accommodate inventiveness by the end-user community in the interests of fostering the originally intended benefits.
- 6.6.3 Recipients of biosamples from biobanks should be required to actively manage any intellectual property generated from their use of the samples, to ensure that discoveries made can be translated into benefit.
- 6.6.4 Such a policy need not detract from the ability of the biobank to operate a policy to limit onward transfer of samples.
- 6.6.5 Similarly, waiving intellectual property rights need not limit biobanks from honouring or acknowledging contributors, or prevent biobanks from requiring end-users to acknowledge the contributions of the biobank, its funders and contributors
- 6.7 Even where property can be claimed as a result of the application of skill as in 6.4.1 above, those holding the product still have moral responsibilities to the original donors to maintain the chains of trust and benefit through sharing of these products in under “reasonable terms” to allow supply to other users.
- 6.8 Difficulties arise when changes occur related to a sample resource such as change of personnel managing a resource / bank, mergers between parent organisations such as NHS Trusts, policy changes by funding bodies, closure of a study management group, etc. Disputes have arisen, for example, when researchers have relocated a sample bank to another institution when changing jobs. In the past, provision for such circumstances has been haphazard and often poorly defined. Individuals or organisations acting as custodians should have plans for maintaining continuity of resources in such circumstances – an “ethical preservation order” should exist over resources.

7. Biosample resources exist to provide a quality service

- 7.1 Quality management should be integral to the management of any biosample resource.
- 7.2 An individual or organisation who does not attend to quality management of the samples and overall resource diminishes the utility of the resource and thus disrupts the chains of trust and benefit.
- 7.3 A commitment to provide a service is necessary in the management of a biosample resource.
- 7.4 An individual or organisation that provides a poor service to donors upstream and researchers downstream diminishes the utility of the resource and disrupts the chains of trust and benefit.

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

8. Human biosample resources should be purposeful

- 8.1 Wherever possible, the collection, storage and distribution of human biological samples for research should be driven by real scientific needs.
- 8.2 The creation of large “stockpiles” of samples for no defined use does have scientific merit, but should not be the operating standard for most banks unless there is very strong justification. This may be the case, for example, for samples from donors with rare diseases where collection over many years in the absence of defined uses is necessary.
- 8.3 Those who manage biosample resources should not be passive participants in the supply chain, but should work to lead opinion and actively promote the merits of research using the resources they hold. This is a prerequisite to the maintenance of the chains of trust and benefit.

9. Biosamples should not be traded as commodities

- 9.1 Human biosamples cannot be owned per se and as such cannot be assigned a monetary “value”.
- 9.2 The processes involved in creating, maintaining and providing the service of biosample resources costs money and it is legitimate for those operating biosample resources to levy fees when supplying samples to others.
- 9.3 Fees may be levied in 2 circumstances:
- 9.3.1 To recover contributions towards the costs (direct and indirect) incurred by the organisation operating the resource.
- 9.3.2 In exchange for services that add utility to the samples (as opposed to “added-value” which, by definition, is not really possible as the samples have no monetary value per se). 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 the boundaries between the types of work of a bank that can only justifiably be charge to recover costs and work which may be deemed as services.
- 9.5 The fees associated with the supply of samples should be related to the actual costs of work required to acquire, store and supply those samples and should not be determined by other “commodity market forces” such as rarity, supply-and-demand, etc that artificially assign values to samples.

10. Summary

- 10.1 There is a widespread belief that the early decades of this century will see intense activity in the field of human research biosample banking worldwide. The reasons for this and the drivers are diverse and will not be discussed further here. However, it is believed that there is a window of opportunity for this endeavour to make its contribution to the advancement of science and the fight against disease.
- 10.2 It is also considered by experts in the field that human research biosample banking needs to “mature” rapidly in terms of ethics, governance, policy and practices to maximise the opportunities that biosample banking can provide for biomedical science, to protect the interests of the donors and to avoid further scandal.

- 10.3 Human biosample banking is a multidisciplinary endeavour that involves diverse stakeholders along a supply chain and many opportunities exist for the spirit, purpose and benefit of the activity to be lost along the chain. Commonly agreed guiding principles based on the need to maintain interlinked chains of trust, benefit and custody along the supply chain, respecting the need for consent and without treating the human body as a commodity, are required.
- 10.4 Well defined and commonly agreed guiding principles for the ethical and legal framework of the management and operation of human research biosample resources are natural accompaniments of an informed, proportionate regulatory environment.