

## **I V .   S P E C I F I C   I S S U E S**

7. In this part, we address and set out our views on specific issues arising out of the practice of research tissue banking and human tissue research.

### **8. Consent Generally**

- 8.1. Full, free and informed consent is the cornerstone of the legal and ethical legitimacy and validity of a gift of human tissue intended for research.
- 8.2. Operators of research tissue banks have an obligation to ensure that valid and appropriate consent to the donation of the gift is obtained.
- 8.3. Consent should be informed and free. Sufficient information on choices and potential consequences, and the unfettered voluntary exercise of free will are the minimum required of an ethically valid consent given by a person of sound mind, full age and capacity. We recognise that there is still some continuing debate as to what constitutes acceptable consent from a legal viewpoint. But we believe that this is an issue that can be readily resolved with appropriate and ethically-informed legal advice and forward planning in advance of the actual taking of human tissues. In this respect, we urge against approaches which place the emphasis on mere technical or formal legal compliance. Those who take tissue must make an honest and common-sense assessment for themselves as to the state of mind of the donor, the sufficiency of the information given to the donor, and the understanding of the donor of that information given to him or her, and finally, the reality of the donor's consent.
- 8.4. We accept that there are circumstances in which it would be impracticable or impossible to insist on consent being obtained. Such a situation may arise, for example, if there is no clear person from whom valid consent can be obtained, and where the donor himself or herself is already deceased, or is legally incompetent to give the requisite consent. Nonetheless, it may be possible in some circumstances for consent to be lawfully given on behalf of the incompetent donor by a legal proxy of the donor. It is beyond the remit of this Report to identify who may stand as valid legal proxies for incompetent donors at law. In any event, the extent and scope of a given legal proxy's lawful authority to give consent may well depend on the particular circumstances, and on the putative proxy's legal relationship with the donor. Where valid consent cannot be given directly by the donor for reasons such as incompetence or incapacity (for instance, if the donor is legally a minor), especial attention should be paid to the ethical and legal validity of any consent taken from the identified legal

proxy for the donor. In such situations, we recommend that, always acting within the limits of the law, the standard protocols and forms to be used in the taking of consent given on behalf of incompetent donors by their legal proxies should be reviewed and settled by the institution's ethics board or institutional review board, acting with the advice of the institution's legal advisors. The same ethics boards and legal advisors may also be consulted for a review of consent formalities in research projects for which it is anticipated that a significant proportion of the donors are or are likely to be legally incompetent.

- 8.5. We are keenly aware that there is an inherent conflict between presenting information to potential donors in a clear and simple way, and between disclosing all the possible kinds of research procedures which may be carried out on the donated human tissue sample, as well as of the benefits which may be derived from it. Inevitably, there must be some compromise between clarity and detail in the drafting of consent forms. We believe that this conflict may be greatly reduced if the consent forms make clear that the intention of the donor is to make an outright gift, with the donor agreeing to renounce all rights whatsoever to and in connection with the gift of the human tissue sample. Framing the request and the consent in this way also properly directs the minds of the donor and the recipient towards the issue of rights in the donated tissue: obviously, both the donor and recipient should be in agreement on this point. We therefore suggest that if a donor is unwilling to make an outright donation, then that proposed donation ought to be declined.
- 8.6. Even in the situation that we suggest, where the donor makes a gift on the basis that it is to be an outright gift, we note that the use of a tissue sample must be governed by the terms of the consent under which the gift was made. Although a donor may make an outright gift of his or her tissue in the sense he or she renounces any property rights to or in connection with the tissue, it is entirely open to the donor to stipulate or define the kind of research uses to which the tissue may be applied. Researchers have a legal and ethical obligation to honour such stipulations. Only research of the kind to which the consent relates (or covers) should be carried out on a given tissue sample.
- 8.7. If it is likely that donated tissue samples will in the future be made available for commercial research with consequent financial benefit or gain to third parties, we suggest that this possibility be made clear to donors at the very outset even if the arrangement is to be that the donors completely renounce their rights to any share of these gains or benefits. In this respect, we note the governing common law principle that informs the letter of the law of both the Human Organ Transplant Act, and of the Medical (Treatment, Education and Research) Act: no person may enter

into a contract for the sale of his body, or any part thereof, including organs, tissue or blood. No person is under any compulsion to give. Nor is any person under an obligation to accept a gift. Again, we emphasise our view that where there is uncertainty as to whether a given potential gift is absolutely unconditional, it would be ethically prudent for a researcher or research tissue banker to decline that gift.

- 8.8. We think that it is unethical to take consent from a donor who may be under the impression (even if such an impression is completely without foundation) that the best efforts made for his or her therapeutic or diagnostic benefit might depend on or be affected by the giving or refusal of consent to the donation. For this reason, where a primary purpose or objective of the taking of the tissue is research, it is important that the consent form for the donation of human tissue samples for research should not form part of the consent form for the taking of the tissue for therapeutic or diagnostic purposes. A physician's objective in taking tissue for therapeutic or diagnostic purposes (or both) from his or her patient is for the welfare and benefit of his or her patient. This objective is an intrinsic and inalienable part of his legal, ethical and professional duty to his or her patient. This objective is quite different from that of a researcher who takes tissue from a donor for the purpose of research. Those who take tissue have an obligation to ensure that prospective donors fully understand and appreciate this fundamental difference in the nature of the objective and purpose between the two kinds of taking, as well as the different uses to which the tissue may be applied. For the avoidance of any conflict of interest (or potential for, or appearance thereof), when tissue is to be taken from a patient with research as one of the primary objectives in addition to therapy or diagnosis, we recommend that separate people should be responsible for the taking of consent for the separate purposes of therapy (or diagnosis, or both), and of research. This means that if research is one of the primary purposes of the proposed taking of the tissue (in addition to therapy or diagnosis), the consent for the taking of the tissue for the objectives of therapy or diagnosis should be undertaken by the donating patient's attending physicians. Then, and separately, consent for the taking of the same tissue and for its use should be the responsibility of the researcher or research team seeking the gift and the use of the tissue in research.
- 8.9. We note, however, that in a large proportion of cases, patients who have tissue removed for therapeutic or diagnostic reasons (or both) are willing to give their informed consent (after being given full information and disclosure) for the archiving or accession of their tissue samples to a research tissue bank for future research after the objectives of therapy or diagnosis are exhausted or satisfied. In these kinds of situation, the primary purpose for the taking of the tissue is clearly therapy or diagnosis.

The purpose of research is only incidental in such cases to the primary purpose of therapy or diagnosis. In such cases, where research is not the primary or immediate objective of the taking, we think that it is permissible for the attending physician who takes consent for the taking of the tissue for therapeutic or diagnostic purposes to also take consent for the use of the tissue, after the therapeutic or diagnostic purposes are exhausted or satisfied, for research purposes.

- 8.10. Blood, urine and other biological fluids which are collected non-invasively without surgery for the purposes of clinical diagnosis may be useful for research purposes. Given the large number of samples routinely taken of blood, urine and other biological fluids for the purposes of clinical diagnosis, we think it would be impractical to require doctors to ask for consent for possible future research use in every case. Exceptionally, we think that the rights of patients in such circumstances can be adequately protected by controls such as requiring appropriate institutional ethics committee or institutional review board approval for applications for research use, and by requiring that such research use do not compromise the confidentiality of the personal information of individual donors (this could be done, for example, through appropriate anonymisation procedures). If the blood, urine or other biological fluids is taken with research as the primary purpose, our observations and recommendations in this Section otherwise apply.
- 8.11. Donors should be free to decide whether their gift should be a general one (in that the gift may be applied towards any research use or purpose), or for a specific (and specified) limited research use or purpose only. Where the intention of the donor is that the gift should be for an unrestricted general research use or purpose, one way of simplifying the procurement of consent may be to have a system in which consent is completely delinked from any particular research purpose. In this system, the donor makes an outright gift of tissue to a specified research tissue bank. The terms of the consent should make it clear that the gift is not to be linked to or be conditional upon any particular research use or purpose. It should also be made clear to the donor that research applications are reviewed and approved by an independent ethics review committee or body. This arrangement may obviate any subsequent argument that the consent given by the donor did not cover the specific research use to which the tissue was subsequently applied.
- 8.12. Such an arrangement would also go a long way to solving the issue of whether “reconsent” is required when tissues originally acquired for a specific research purpose is subsequently sought for use in another, and there is doubt as to whether the original consent covers the subsequent use.

- 8.13. It is beyond our remit for us to suggest how the requirements of valid consent may be formally met. We cannot prescribe the particulars of how consent should be obtained, and we take the view that it is the responsibility of institutions to work out their own consent procedures and consent forms with their legal advisors, and to train their staff accordingly.
- 8.14. In taking the consent, especial attention is necessary to ensure that donors fully understand what is proposed to be taken, particularly if gross human tissue samples (e.g. entire organs or blocks of organs, or of limbs, as opposed to tissue slides or small tissue blocks) are involved. Gross human tissue samples may be viewed in a very different light from small human tissue samples by the public. The issue of respectful and appropriate methods of disposal for such gross human tissue samples may have to be considered by the custodians of such samples when they are no longer needed and de-accessed from the bank or collection. Researchers and institutions having responsibility for the custody, use and disposal of such tissues should at all times be sensitive to social, cultural and religious sentiments relating to the treatment, use and disposal of such tissues.
- 8.15. We also think that researchers and tissue bankers should bear in mind that consent to the taking, and consent to particular uses are two quite separate things. Consent given for the taking of tissue for a specific purpose does not necessarily authorise the use of the tissue for a different purpose.
- 8.16. Similarly, human tissue taken originally under statutory authority (for example, a post-mortem examination carried out on the authority of the State Coroner) for a statutory purpose, should not be used for other purposes once the statutory purpose has been exhausted, unless consent has been obtained for uses not covered by the statutory authority.
- 8.17. At law, a failure to take consent for taking of tissue may not only amount to a civil wrong (a tort), but in some circumstances may also amount to a criminal offence. The current law is less clear in relation to very small samples taken without any invasive methods (for example, by the interception of material intended for disposal). In this regard, we note with interest the recent recommendation made by the UK Human Genetics Commission that “consideration be given to the creation of a criminal offence of the non-consensual or deceitful obtaining and/or analysis of personal genetic information for non-medical purposes”<sup>1</sup>.

---

<sup>1</sup> UK Human Genetics Commission, Inside Information: Balancing interests in the use of personal genetic information May 2002.

## **9. Consent and Legacy Tissue Collections**

- 9.1. A special difficulty faced by tissue banks in Singapore and in the rest of the world is posed by the existence of large collections of tissue samples accumulated over many years for which no specific or adequate consent for research investigations has been obtained. In the vast majority of the cases, the original donors can no longer be reliably traced for consent to research, or such tracing may no longer be practicable or socially acceptable (for instance, in the case of very old collections in which there is a strong likelihood that many of the donors may have since died, especially if the sample tissues were originally taken for diagnostic purposes in relation to conditions such as cancer). We refer to these collections as legacy tissue collections.
- 9.2. These legacy tissue collections, by virtue of their sheer size and range of coverage, are often very valuable to academic and commercial researchers alike.
- 9.3. While some have advocated the extreme view that no research use should be made of these legacy tissue collections, we take the view that it is not in the wider public interest to suggest a blanket ban on access to these collections by researchers. We take the view that it is unreasonable to expect those who have assembled such collections in good faith for the advancement of medical knowledge to have divined the importance now placed on consent.
- 9.4. We take the practical approach that tissue collected in good faith at a time when there was a lack of any clear ethical, professional or legal guidelines governing the collection of such tissues is not something to be condemned: it is not the fault of medicine that the law and bioethics often lags very far behind the reality of medical practice and technology. In the absence of guidance from the law, or from an established canon of bioethics, medical workers and researchers can only act in good faith according to the best professional practices of the day.
- 9.5. On this basis, we take the view that it is consistent with good stewardship to allow reasonable and respectful research use of such legacy tissue collections for the greater public good.
- 9.6. It is one of the recommendations advanced by us in this Report that steps should be taken to formulate a national ethical policy governing research access to such legacy tissue collections. There may be a possibility that legislative intervention may be necessary to cure the defect stemming from problems with the lack of consent. Otherwise, the scientific value of these legacy collections may be severely impaired by the need to maintain

separate access guidelines for legacy tissues and those tissues for which appropriate and adequate consent has been obtained.

## 10. Confidentiality

- 10.1. Confidentiality lies at the heart of the physician-patient relationship. A common theme of the position papers and representations submitted to us is the acceptance, as a fundamental controlling principle, of the donor's right to privacy and confidence.
- 10.2. In relation to genetic information derived from human tissue, the obligation of confidentiality is one which is universally recognised. Article 7 of the 1997 UNESCO *Universal Declaration on the Human Genome and Human Rights* requires that "[g]enetic data associated with an identifiable person and stored or processed for the purposes of research or any other purpose must be held confidential in the conditions set by law". The World Health Organisation has proposed that "[g]enetic data should be treated as confidential at all times. Genetic data should only be used to advantage and empower an individual or family, and for better treatment or prevention of disease. Data relevant to health care should be collected and kept by medical geneticists in secure confidential files"<sup>2</sup>.
- 10.3. We agree that researchers and research tissue bankers alike have an obligation to protect the confidence and privacy of donors.
- 10.4. We further note that the general obligation of confidence is one which is protected by the general common law principles applicable in Singapore. In certain specific circumstances, some aspects of the obligation of confidence may be mandatory under statute.
- 10.5. Confidentiality and consent are closely interlinked and interwoven issues. The common ground between them is that both spring from the obligation to protect and respect the dignity and autonomy of patients and donors. In this respect we note that the UK Medical Research Council has examined confidentiality issues in medical research at length in their report on *Personal Information in Medical Research* (October 2000).
- 10.6. The MRC took as their first governing principle that:  
"Personal information of any sort which is provided for health care, or obtained in medical research, must be regarded as confidential. Wherever possible people should know how information about them is used, and

---

<sup>2</sup> World Health Organisation, Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetic Services 15-16 December 1997 (WHO/HGNG/GL/ETH/98.1).

have a say in how it may be used. Research should therefore be designed to allow scope for consent, and normally researchers must ensure that they have each person's explicit consent to obtain, hold and use personal information. In most clinical research, this is practicable."

- 10.7. In our view, however, the requirements of consent and confidentiality should not be applied inflexibly and blindly to all circumstances. If the central common purpose of the general obligations of consent and of confidentiality is the protection of and respect for the dignity and autonomy of patients and donors, then there may be special circumstances in which specific departures from the general rule of these two obligations may be permissible, so long as the central common purpose of the obligations is preserved.
- 10.8. For example, strict adherence to the principle of privacy and confidentiality may be difficult to square completely with other equally compelling objectives. In other cases, it may be difficult or impossible to recontact the donor or the donor's family for consent (or re-consent) to further research, or it may be socially unacceptable to do so (for example, if there is a strong likelihood that the donor may be dead). We think that in these and in other situations where consent or re-consent may be impossible or difficult to obtain, it is permissible for researchers to consider the use of anonymised data arrangements or data-escrow arrangements as may be approved by appropriately-constituted ethics boards or institutional review boards.
- 10.9. In these and other similar arrangements, the object is to preserve the confidentiality and privacy of the donors. The central common purpose of the general consent and confidentiality requirement is not compromised. We recommend the use of such arrangements where practicable, and where the scientific objectives of the proposed research will not be compromised.

## **11. Approaches to Governance**

- 11.1. Given the current pace of developments in the genetic and genomic sciences, we do not think that it is appropriate to resort to hard-coding specific rules in legislative form for the regulation of research and commercial activity in the genetic and genomic sciences. Overly-specific rules run a risk of rapid obsolescence, and of abuse by those minded to be seen to comply only with the letter but not the spirit of the law.
- 11.2. In general, we recommend legislative intervention only in situations where it is clear that effective professional self-regulation and a fair balance of

rights and interests between individuals and the public in encouraging research cannot be achieved without legislative teeth.

- 11.3. We think however that there is a role for carefully targeted legislative assistance in the form of enabling legislation (as in our suggestion in relation to the statutory remedying of consent for research access to legacy tissue collections), and in empowering appropriate Government agencies to exercise a supervisory jurisdiction as gatekeepers over certain kinds of activities in relation to research tissue banking.
- 11.4. In the context of the genetic and genomic sciences, we note that one particularly obvious gateway is the research tissue bank itself. Researchers, whether they be commercial or academic researchers, and whether they be currently regulated under the various medical Acts or by the Ministry of Health, require access to collections of physical tissues for their work. This being the case, we suggest that appropriate legislation for the control and supervision of this gateway, through the appropriate Government agency being given an approval and supervisory jurisdiction over the establishment and conduct of research tissue banking, would be a flexible and efficient means of basic control over the genetic and genomic sciences in Singapore. An important advantage of such a regime would be that non-medical researchers (who are not subject to the current provisions of the Private Hospitals and Medical Clinics Act) and medical researchers alike would be subject to the same set of such operational and ethical guidelines as may be imposed by the appropriate authorities, and thereby operate on a level playing field.
- 11.5. In the HSR Report, we recommended (in Recommendation 8 of the HSR Report) that a statutory authority be set up to license, control and monitor all human stem cell research conducted in Singapore. If such a statutory authority is to be eventually established for the regulation of human stem cell research, it may be appropriate for this statutory authority to be given the supervisory and licensing jurisdiction over research tissue banks in Singapore as well. Such a statutory authority should be given sufficient powers of direction, enforcement and supervision, so as to enable it to effectively give ethical and legal direction for the conduct of research tissue banking in Singapore, to ensure compliance with such direction, and such other relevant rules, standards and codes of conduct, to establish and maintain proper operational governance, as well as to protect the interests and rights of patients, donors and their families.
- 11.6. As explained in Section 5, our preference and recommendation is for a system which emphasises institutional responsibility and good internal self-governance, and the promotion of adherence to the spirit rather than to the letter of the law. We think this can be best achieved through the

licensing of responsible institutions with proven and acceptable systems of self-regulation rather than through the direct regulation of individual researchers and tissue collections by the statutory authority.