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CONSULTATION PAPER
HUMAN TISSUE RESEARCH

THE BIOETHICS ADVISORY COMMITTEE
SINGAPORE

27th February 2002

THE BIOETHICS ADVISORY COMMITTEE

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About the Bioethics Advisory Committee

The Bioethics Advisory Committee ("the BAC") was appointed by the Singapore Cabinet in December 2000. The BAC was directed to "examine the legal, ethical and social issues arising from research on human biology and behaviour and its applications" and to "develop and recommend policies ... on legal, ethical and social issues, with the aim to protect the rights and welfare of individuals, while allowing the Life Sciences to develop and realise their full potential for the benefit of mankind".

The BAC reports to the Ministerial Committee for Life Sciences. For further information about the BAC and its work, please visit <http://www.bioethics-singapore.org>

Contacting the Bioethics Advisory Committee

The BAC welcomes views, comments, suggestions and other feedback on the issues raised in this and other consultation papers, or on any bioethical issue within its remit. All feedback should be addressed to:

Bioethics Advisory Committee
250 North Bridge Road, #15-01/02,
Raffles City Tower,
Singapore 179101

I. INTRODUCTION

1. About this Paper and the consultation process

- 1.1. This Consultation Paper on Human Tissue Research (the “**Paper**”) is issued by the Bioethics Advisory Committee, Singapore (BAC) as part of its efforts to obtain professional and public feedback on the issues outlined in this Paper. The feedback and suggestions received by the BAC will help inform and shape the recommendations which the BAC will be making to the Government.
- 1.2. Human Tissue Research is a broad field of inquiry. This Paper is not intended as an exhaustive survey. Instead, we propose to focus on a few specific issues arising out of the practice of human tissue banking which we think require resolution as a matter of priority. Other issues (some of which are also identified in this Paper) may be addressed at a later time in separate consultation papers.
- 1.3. We have made preliminary recommendations on issues where we think such recommendations may be reasonably and confidently advanced. We invite views, comments, suggestions and other feedback on the preliminary recommendations outlined in this Paper, and on such other issues as we may have identified in this Paper.
- 1.4. The recommendations in this Paper are intended primarily as a springboard for discussion, and do not necessarily represent the final recommendations which the BAC may make to the Government.

2. Definitions

- 2.1. In this Paper, we use the term “**human tissue**” to refer to all kinds of human biological materials derived from living or cadaveric donors, including solid body tissues, organs, foetuses, blood and other body fluids and their derivatives, cord blood, embryos, gametes (sperm or eggs) or any part or derivative thereof.
- 2.2. As blood banking is already well-regulated in Singapore, we exclude **blood banking for therapeutic purposes** from the ambit of this review, and do not include it in our definition of “**tissue banking**”. However, we do include in our definition research involving studies of blood collections (whether the original samples were collected for therapeutic or research objectives, or a

combination of both) or the use of such blood samples or their derivatives for purposes other than direct therapeutic ones such as transfusions.

- 2.3. The recommendations set out in this Paper are intended to apply generally to all human tissue as defined above, with the caveat that account should be taken of specific recommendations which the BAC may have made or may make in relation to human embryos, cord blood, gametes and stem cells in its separate report and recommendations on **human embryonic stem cells and human cloning**.

3. Formulating Principles

- 3.1. In recent years, much public attention has been focused on developments in the new life sciences, and on genetic and genomic research in particular. These new life sciences offer enormous promise of potential benefits.
- 3.2. In many of the current thrusts of the new life sciences, researchers are entering completely new grounds which raise many novel legal, ethical and social issues. Consequently, the body of community ethics is being asked to offer ethical direction and guidance for the ethical conduct of research in entirely novel situations for which there are no readily available precedents. In many areas too, the state of the law sometimes lags far behind the realities of the current and future state of technology, so that practitioners and researchers in the new life sciences must act in the absence of clear legal guidance.
- 3.3. We believe that, in this respect, the development of sound ethical principles which are acceptable to and supported by the community at large will assist in the formulation of the law in areas and for situations where this is eventually felt to be necessary. Such a body of sound ethical principles will also serve as the common understanding on which ethical research work may be carried out.
- 3.4. We take the view that the vast majority of scientists and researchers are responsible and are acutely aware of potential ethical concerns in the work that they do, and in that which they may propose to carry out. Most wish to do what is ethically right. Indeed, many may be inhibited from participating in some areas of research (which may in fact be entirely acceptable to the community, and in the public interest) by the lack of clear ethical direction or agreement on a given point, or by uncertainty generated by controversy in related areas.
- 3.5. Where there is broad agreement in leading jurisdictions on applicable principles, we have in general tended towards recommending the adoption of

these principles. It is only recently that various developed jurisdictions have embarked upon the task of the formulation of guidelines and rules for the governance of the new life sciences, and to examine the ethical issues involved. In some areas, an international consensus is beginning to emerge. But in many other areas, the future shape of the body of ethics is still being debated. It is hoped that the feedback received by the BAC on this Paper will help advance that process. For these reasons, too, the recommendations which we make at the end of this Paper are advanced as Interim Recommendations, pending the emergence of a clearer body of consensus and direction internationally in the areas under discussion.

I I . H U M A N T I S S U E R E S E A R C H

4. The Role and Promise of Human Tissue Research

- 4.1. Research involving the use of human tissue, or the use of information derived from such human tissue, is a fundamental cornerstone of modern medical research and knowledge. Many of the advances in the life sciences which have contributed so much to our health, physical well-being and long life expectancy are founded on knowledge gleaned in one way or another from human tissue research. For instance, vital epidemiological information about the pattern and incidence of occurrence of various forms of diseases such as cancers has been (and continues to be) gained from human tissue research, and through the analysis of such information, important discoveries about the prevention, control and treatment of such diseases have been made for the benefit of humankind.
- 4.2. In the future, human tissue research is likely to assume a more important role as new uses for the information derived from such research are discovered. Most notably, almost all forms of genetic and genomic research use human tissue, directly or indirectly, as the starting point of their investigations.
- 4.3. Although tissue banking in some form or another has been practised for well over a century, it is only in the last decade that tissue banking has come into the public limelight with the recent surge of interest in the new life sciences, and in particular, in the fields of human genetics and genomic research.
- 4.4. In the past, human tissue collection and banking has arisen largely as an incidental adjunct to the collection of human tissues primarily for diagnostic procedures and pathological examination. These collected tissues were put to research purposes after their primary purpose was exhausted. Through this process, however, a great deal of extremely valuable information was gained

for the advancement of medical science and public benefit. With the rise of the new life sciences, and in particular in the context of recent advances in the fields of human genetics and genomic research, tissue banks and collections have assumed a new importance.

- 4.5. At the heart of the matter is the fact that research involving the study of human tissue samples, or of the information gleaned from such research, or both, lies at the very foundation of nearly all lines of genetic and genomic research and enterprise.
- 4.6. Even given the likelihood of at least some dead ends and over-optimistic media hype in the emerging fields of human genetics and genomic research, there is a general consensus that many of the answers and solutions to some of the most intractable medical and public health problems are likely to emerge from genetic and genomic research and enterprise in the near future. Apart from providing therapeutic advances, the genetic and genomic sciences now offer exciting new prospects in the field of preventive medicine, especially through advances in genetic screening.
- 4.7. In this Paper, we attempt to canvass some of the issues which we think need to be eventually addressed for the establishment of a sound ethical, legal and social foundation for the proper conduct of human tissue banking and research in Singapore for now and for the future.

5. Human Tissue Banking In Singapore

- 5.1. In the past, human tissue banks in Singapore have been built up largely as an incidental by-product of diagnostic procedures. Most commonly, human tissue samples would be removed during surgery or other medical procedures and processed for pathological examination and investigation. For example, suspected tumours would be preserved or fixed in the form of paraffin blocks to facilitate further pathological investigation. These tissue collections largely comprise tissue slides, paraffin blocks and tissue preserved with wet preservation techniques. These techniques generally render the cellular material non-viable. Some large collections, mostly institutional, have been assembled in this way.
- 5.2. Pathologists in Singapore have traditionally taken (and continue to take) the view that this retention is on the basis that these tissue samples forms part of the medical records of the donor, and that they (and the institutional host for the collection) are “stewards and guardians” or custodians of these tissue samples on behalf of the donors.

- 5.3. Human tissues are collected not only from living donors, but also from the dead. Cadaveric tissue samples are also collected in the course of coronial or consensual autopsies for the purposes of diagnostic procedures.
- 5.4. On completion of the pathological investigations, these tissue samples (from living and cadaveric donors alike) are generally archived and added to the human tissue collection. The Chapter of Pathologists of the Academy of Medicine, Singapore, states that this is done “in accordance with current good clinical practice guidelines, [so that] the case files (in this case [the] slides and blocks) can be reviewed and perhaps sent for expert opinion. The tissue is kept against the chance that there may be a medico-legal challenge regarding the diagnosis or [in the case of living donors] the possibility that new prognostic and therapeutic markers may be developed, and used during the patient’s lifetime”.
- 5.5. The largest collections of these kind of **“incidental” tissue banks** are generally held by hospitals, teaching centres and large health institutions, although some much smaller “private” collections held by individuals or groups of individuals apparently do exist. These “private” collectors may be specialist physicians or medical researchers with research interests in specific medical conditions. In some of these cases, these private human tissue collections have been accumulated on the principle that the referring physician has the right to the possession or at least the return of the human tissue sample.
- 5.6. Currently, there are no clear guidelines as to whether referring or sending physicians have a right to demand the return of these tissue samples.
- 5.7. In general, our view is that human tissue collections by private individuals should not be encouraged, and that, as far as possible, tissue banks should be held by institutions (for example, by a hospital, a university or a research institution). Such institutions may be of a public (e.g. a teaching hospital) or private (e.g. a private hospital, or a private commercial research venture) character. If non-institutional collections have to be made for any reason (for example, collections of a specific kind of tissue pursuant to a specific research project), such collections should only be assembled on the understanding that the human tissues collected will eventually be consolidated with the larger collections of institutions. Institutional human tissue holdings need not be physically centralised. It would be sufficient, for example, for an institution to have in place a current database of all human tissue holdings within that institution. Such a database could be part of the institution’s database of research projects, with information fields such as the research area, disease, human tissue collected, where they are stored within the institution, and the units and persons responsible for these human tissues.

- 5.8. Consolidation of smaller human tissue collections in larger institutional holdings confers many benefits. A larger institution has more resources for the proper maintenance and stewardship of the human tissue samples under its charge. Continuity and preservation of the human tissue samples are also assured, and there is a greater likelihood of their being available to a wider pool of researchers. By itself, the size of holdings is also an important benefit of consolidation: a large-scale collection is more useful (particularly for population studies) than a small and limited collection.
- 5.9. In recent years, however, tissue banking in Singapore has moved beyond the merely incidental towards **purpose-assembled research banks**. In this kind of tissue bank, human tissue is collected purely or primarily for the purpose of research, and not merely as an incidental benefit of diagnostic procedures.
- 5.10. There has also been a parallel trend towards the establishment of collections of human tissue in which the biological material remains viable or potentially viable, at least in some respects, at the cellular level. For instance, human tissue samples may be flash-frozen, and/or living cell lines may be propagated on culture media. This greatly increases the value of the samples for many lines of research.
- 5.11. We take the view that such purposed-assembled research banks are to be encouraged, provided that all appropriate ethical and legal considerations and concerns are appropriately met and addressed, as they promote and enhance research, which offers the promise of immense benefit in the future for humankind.

I I I . L A W & P R A C T I C E

6. Current Law

- 6.1. There is currently little in the way of law (either common law or statutory law) governing some of the most fundamental questions in relationship to tissue banking in Singapore.
- 6.2. In respect of donations of cadaveric tissue, Parliament has provided a statutory mechanism for donation in the form of the Medical (Therapy, Education & Research) Act. This enables people to state in advance their intention to donate their bodies, organs or tissues for research or for transplantation after their death. It also enables the family of a deceased

person to donate the body, organs or tissues for research or for transplantation.

- 6.3. In relation to gifts by *living* donors, there is currently very little guidance in the way of either the statutory law or common law, outside of some provisions in the Human Organ Transplant Act.
- 6.4. Currently, the only express statutory provision for the governance and regulation of tissue banking is to be found in the Private Hospitals and Medical Clinics Regulations 1993. These Regulations provide that where a “private hospital” (no mention is made of individuals, or of private clinics or research laboratories) proposes to perform certain specified specialised procedures or services, prior approval of the Director of Medical Services must be obtained at least 30 days in advance. “Tissue banking” and “sperm banking” are included in the list of specialised procedures or services which require such approval. Tissue banking is not defined in the Regulations, or in the parent Act, or indeed in any other statute. Neither the Regulations nor the parent Act spell out any guidelines for the proper conduct of tissue banking.
- 6.5. At the present time, there does not appear to be any uniform approach to the governance and regulation of tissue banking internationally. The Draft Discussion Document entitled *Data Storage and DNA Banking for Biomedical Research: Informed Consent, Confidentiality, Quality Issues, Ownership, Return of Benefits: A Professional Perspective* issued by the Public and Professional Policy Committee of the European Society of Human Genetics as part of the EUROGAPP Project 1999-2000 offers an illuminating survey of the gamut of existing opinions, legislation, guidelines and other policy statements applied in or issued by EC institutions, 18 European countries, the United States, and international organisations. Except in the case of the United States, and possibly France, the majority of the jurisdictions surveyed are notable more for the absence of specific agreed national guidelines or legislation than by the presence of such in relation to storage of data derived from human tissue research and DNA banking.
- 6.6. For the present time, the BAC concludes that a full consensus on many issues has yet to emerge on many of the most critical issues in relation to human tissue banking. The most intractable problems in this regard are the issues of property, control and ownership rights to tissue samples.
- 6.7. We think, however, that it is desirable that a review be undertaken of the law governing this area, and a professional and public dialogue initiated to discuss the ethical and social considerations which should inform the shape of the law in this area.

- 6.8. Legal review has recently acquired a new urgency in light of moves by other countries to clarify their own laws on human tissue banking with the new interest worldwide in the new life sciences. Increasingly, the harmonisation of laws and rules in this field is likely to emerge as an important consideration in shaping the laws and rules in each jurisdiction. In a world where large-scale collaborative research projects tend to transcend national borders, there is an increasing likelihood that many countries may demand proof of each other that there is approximate equivalence in the degree of ethical and legal protection or regulation before they will allow the cross-frontier transfer of research data, or allow cross-border research collaboration which involves access to their national tissue collections or data. For example, Singapore researchers may be asked to demonstrate that their protocols for the safeguarding of the confidentiality of data meet the standards of the jurisdictions in which their proposed collaborators are based. Failure to achieve such standards locally may well mean that Singapore researchers may be excluded from opportunities for collaboration with researchers in those jurisdictions (which include most developed countries).

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

7. In this section, we address and set out our views on specific issues arising out of the practice of human 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. We take the view that, where it is practical to do so, tissue bankers have an obligation to obtain consent to the donation of the gift.
- 8.3. 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.
- 8.4. 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 gift is to be an absolute one, with the donor renouncing all rights whatsoever to and in connection with the gift of the human tissue sample.

- 8.5. If there is any possibility that donated tissue samples may in the future be made available for commercial research with consequent financial benefit or gain to third parties, then this possibility must 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.
- 8.6. Consent should be informed and free. It would be 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.
- 8.7. For this reason, we think 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. We recommend that, where possible, the person responsible for explaining the nature of the donation and the taking of the consent for the donation should not be the person who receives the consent for the taking of the tissue for therapeutic or diagnostic purposes.
- 8.8. Another way of simplifying consent is to have a system in which consent is completely delinked from the research purpose. In this system, the donor makes an absolute gift of tissue to a specified tissue bank. But it is made clear to the donor that the consent to the gift is not to be linked to or conditional upon any particular approved research use or purpose. It is also made clear to the donor that research applications are handled 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.
- 8.9. 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.
- 8.10. 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. In such situations, we recommend that, acting within the limits of the law, the decision for the taking of the human tissue from such a person should be referred to an appropriately constituted ethics board or institutional review board.

8.11. 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.

8.12. 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.

8.13. Similarly, it should not be assumed that human tissue taken without consent, even though under statutory authority (for example, a post-mortem examination carried out on the authority of the State Coroner), may be used for other purposes once the statutory purpose has been exhausted.

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 have 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 the 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 interim recommendations advanced by us in this Paper that steps should be taken to formulate a national ethical policy governing research access to such legacy tissue collections. The formulation of such a policy should be led by a national-level body. There may be a possibility that legislative intervention may be necessary to cure the defect stemming from problem 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 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 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 process 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”¹.

- 10.3. We agree that the researchers and 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 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 rules of these two obligations may be permissible, so long as the central common purpose of the obligations is preserved.

¹ 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).

- 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 board 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 human tissue banking.
- 11.4. In the context of the genetic and genomic sciences, we note that one particularly obvious gateway is the 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 tissue banking, would be a flexible and efficient mean of basic control over the genetic and genomic sciences in Singapore.

- 11.5. We especially think that, for example, the jurisdiction of the Director of Medical Services under the Private Hospitals and Medical Clinics Act could be extended to all individuals or bodies (and not just healthcare establishments, hospitals, medical clinics and clinical laboratories) minded to engage in the conduct of tissue banking. Such a supervisory jurisdiction would place non-medical researchers (who are not subject to the provisions of the Act) and medical researchers alike on a level playing field and subject them to the same set of such operational and ethical guidelines as may be imposed by the appropriate authorities.
- 11.6. Alternatively, if a statutory agency is eventually established for the regulation of stem cell research (as has been suggested by the BAC), it may be appropriate for such a statutory agency to be given regulatory jurisdiction over human tissue banking in Singapore as well. Such a statutory agency 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 all forms of tissue banking carried out 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 to protect the interests and rights of patients, donors and their families.
- 11.7. We take the view that it is desirable to have consistent and transparent rules and standards which should have common application to all forms of tissue banking in Singapore, whether carried by the private or public sector, and whether such tissue banking is carried out primarily or incidentally for the purposes of research, and whether such research is for a commercial end or for a non-profit end.
- 11.8. In the interest of promoting accountability and transparency, we think that a national-level committee or consultative body comprising experts from relevant industrial, academic, research and professional sectors of the life sciences, together with appropriate representation from the public, could assist in formulating a sensitive and flexible approach to regulation.
- 11.9. To take this proposal further, such a national committee could assume the role of a national ethics review board which would be responsible for the formulation of national policy relating to the regulation, conduct and governance of tissue banking in Singapore. For this purpose, it could be constituted to advise the proposed statutory agency accordingly.

11.10. A further role that such a national committee might assume could be the oversight of the decisions of institutional review boards or institutional ethics committees on applications by researchers for access to human tissues. The national committee could review these decisions to ensure that common standards are applied nationally by such institutional review boards or institutional ethics committees. By the same token, the institutional review boards or institutional ethics committees could be given representation either on the national committee itself, or a standing professional standards forum of the national committee.

11.11. Such a national committee or consultative body could also help formulate other non-legislative informal aspects of regulation, such as the specific rules or codes of conduct and operational codes by which human tissue banks in Singapore may agree to be bound.

V . I N T E R I M R E C O M M E N D A T I O N S

12. In this section, we set out our preliminary recommendations arising out of the matters discussed above. We emphasise that these are only interim recommendations: human tissue banking is a rapidly evolving field in Singapore, and we expect that over time, new issues and new questions in the social, ethical and legal spheres will arise and require resolution. We also emphasise that not all the issues raised in this Paper can find a ready solution in either ethics or the law, let alone both, and that some of them can only be resolved after further professional and public debate and dialogue, and with a better understanding of the issues involved, as well as the needs and concerns of the relevant participants.

13. **WE RECOMMEND THAT:**

Recommended Ethical Principles

13.1. As a starting point for this dialogue, we recommend the adoption of the following principles²:

² A number of these principles are adapted from the Report of the UK Medical Research Council entitled Human Tissue and Biological Samples for Use in Research: Operational and Ethical Guidelines (January 2001).

Primacy of the Welfare of the Donor.

13.1.1.1. The health, welfare and safety of the donor shall be the paramount consideration in the taking of any tissue. Where tissue is being taken primarily for a therapeutic or diagnostic purpose, the secondary purpose of taking tissue for research, or the way in which the tissue is taken for research, should not be allowed to compromise or prejudice in any way the primary purpose of the taking. Where a tissue sample has been taken primarily for the purposes of diagnostic procedures, no further sub-sample should be taken from the main sample for the purposes of research until the diagnostic procedures are satisfied, or unless the diagnosing pathologist certifies that the taking of the sub-sample will not compromise the main diagnostic purpose of the taking of the main tissue sample. Where the taking of the tissue is primarily for the purpose of research, such taking and research should only be proceeded with if the potential benefits of the taking outweighs the potential risks to the patient. All living donations involve some degree of risk to the donor, although in the vast majority of cases, this risk will be negligible.

Informed Consent

13.1.1.2. No tissue shall be taken, or shall be accepted, unless the full, free and informed consent of the donor has been obtained. Our remarks in the section on Consent above applies, as well as the exceptions noted thereto.

13.1.1.3. We also recommend that patients should be informed when material left over following diagnosis or treatment (described as surplus to clinical requirements), might be used for research. Patients may be under the expectation that any waste tissue will be disposed of appropriately, and may object to the use of such tissues for research.

13.1.1.4. Special attention should be paid to the legal and ethical resolution of consent issues in relation to legacy tissue collections. Where such resolution cannot be satisfactorily achieved, we recommend separate regimens of access for the legacy and non-legacy portions of a tissue bank holding both kinds of tissue. We repeat our comments in relation to legacy tissue collections in the section on Consent and Legacy Tissue Collections above.

13.1.1.5. We recognise, however, that there are arguments that in specific situations it may be ethically acceptable to proceed without consent provided that sufficient precautions are taken for the protection of the privacy of the patient and the patient's family. For

instance, this may be achieved through appropriately constructed anonymization procedures or data escrow arrangements. We also recognise that it may be impractical to apply the principle of informed consent in its full force to legacy tissue collections, or to tissue banks in which the legacy material cannot be reliably separated. In these cases, a national ethical policy may have to be worked out as suggested in paragraph 9.6 above.

13.1.1.6. Tissue banks should develop and have in place electronic database systems that will enable the consent status and consent conditions (if any) of every human tissue sample.

Respect for the Human Body

13.1.1.7. Ethics, the law, and the cultural and religious traditions of our society are all in agreement with the principle that the human body and its remains are to be treated with respect. Researchers and tissue bankers need to be sensitive to religious and cultural perspectives and traditions, and should in particular be aware that whole cadavers or gross organ parts are viewed in very different light from small tissue samples by lay persons. Researchers and tissue bankers should always ensure that donors and the families of donors fully understand the extent of the intended gift. For example, the term “tissue” should not be used without further elaboration and explanation if it is intended that organs or substantial parts of organs are intended to be taken. Especially in the case of gross tissue samples, donors or their families should be consulted in advance of the donation as to their wishes for the appropriate disposal or return of surplus tissues when these are no longer required.

Donations to be Gifts

13.1.1.8. Donations of tissue samples for use in research should be treated as outright gifts. Donors should not be paid any financial incentives for the donation, although they may be given reasonable reimbursement of any expenses incurred in the donation of the sample. As a corollary of this principle, donors should not expect any personal or direct benefit from the donation of tissue, including information of any medical condition or predisposition or likelihood of such discovered in the course of research on the sample. Likewise, researchers and tissue bankers should not be under any obligation to disclose such information to the donors, unless they have agreed to do so in advance of the donation. Where appropriate and possible, it may be desirable to ask for consent to be given for any and all research purposes as may be approved by a properly-constituted ethics committee or institutional review board in

accordance with any rules, standards or codes as the relevant authority may lay down. To this end, an effort must be made in good faith to give the donor or the donor's family a fair picture of the principal uses which the tissue is likely to be put to, with the caveat that new uses not within current contemplation or practice may and are indeed likely to arise in the future.

Ethical Review of Research Proposals and Access Requests

13.1.1.9. All research using human tissue samples should be approved by an appropriately constituted research ethics committee or institutional review board. Especial attention must be paid to the independence and integrity of such committees or review boards, and any conflict of interest (whether real or potentially real, or even the semblance of a conflict of interest, even if such semblance is in fact unfounded) should be scrupulously avoided. The appointment, and constitution of such ethics committees or review boards should be as transparent as is practicable.

13.1.1.10. A national-level committee or consultative body comprising experts from relevant industrial, academic, research and professional sectors of the life sciences, together with appropriate representation for the public, should be formed to assist in formulating a sensitive and flexible approach to regulation.

13.1.1.11. This national-level committee could take the form of the national ethics body suggested by us in paragraphs 11.8 to 11.11 above. Such a national ethics body would also serve the function of fostering common standards and approaches among individual institutional review boards or ethics committees in Singapore.

Confidentiality

13.1.1.12. Researchers and all those involved in the conduct of tissue banking have an obligation to protect the confidentiality of the personal information of donors entrusted to them, as well as the privacy of donors. Consent must be obtained from the donor (or from his family, if deceased) for the release of any personal information to researchers or to any third party.

13.1.1.13. Researchers and all those involved in the conduct of tissue banking also have an obligation to protect the confidentiality of personal information given to them by donors about other individuals who are not themselves donors, as well as the privacy of such individuals. Scientifically valuable information is often given by donors of tissue samples which may relate to individuals other than the donor himself or herself. Commonly, a donor may be

asked to provide details of the medical history of family members. Researchers should recognise that such information and such individuals should be accorded the same respect and protection as accorded to the donor.

Institutional Tissue Banking

- 13.2. Subject to our views as set out in paragraphs 5.5 to 5.8 above, tissue banking should be conducted only by institutions such as may be approved by the appropriate authorities to do so, and not by private individuals or groups of private individuals.

Ethical Governance of Operational Aspects of Tissue Banking

- 13.3. There should be statutory regulation and supervision of all forms of tissue banking, and a statutory authority should be constituted for this purpose. No tissue banking should be carried out without the licence of the statutory authority. The 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 all forms of tissue banking carried out in Singapore, to ensure compliance with such direction, and such other 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.
- 13.4. Institutions that conduct tissue banking should have in place transparent and appropriate systems and standards for the proper ethical, legal and operational governance of tissue banking.
- 13.5. Such systems and standards might include, but need not necessarily be limited to:
- 13.5.1. The formulation of clear and transparent written ethical guidelines and policies for the operation of tissue bank and the governance of their tissue banking activities;
 - 13.5.2. The formulation of clear written Standard Operating Procedures for the day-to-day operations of the tissue bank, with especial attention being paid to ensure the integrity and biological safety of the tissue holdings;
 - 13.5.3. The establishment of an appropriately constituted research ethics committee or institutional review board to oversee requests for research access to or the use of human tissues, on clear, objective and transparent criteria;

- 13.5.4. The provision of a proper system for periodic and impartial census and audit, and a proper inventory system for their tissue holdings and for research accesses to the holdings;
- 13.5.5. In consultation with their legal advisors, the working out of simple and clear procedures and proper documentation of the required consent process;
- 13.5.6. The establishment of clear and written policies for the sharing of tissue bank resources with other tissue bankers and researchers;
- 13.5.7. The establishment of written procedures and policies for the culling and appropriate disposal of unneeded human tissue samples from the bank;
- 13.5.8. The establishment of legally and ethically adequate and acceptable systems to protect and safeguard the confidentiality of personal information of donors, and the privacy of such donors and of any other individuals (not being donors themselves) whose identity or personal particulars to which such information may relate; and
- 13.5.9. The establishment of a system for the periodic reporting of activities to those who have overall responsibility of the larger institution to which the tissue bank belongs.

Initiating An Ethical Dialogue

- 13.6 A professional and public dialogue be initiated to settle the principles which should guide the conduct of tissue banking. While we expect that most of the input in the dialogue will come from professionals in the life sciences, we also recommend that the views of the public be sought. This Paper is issued by the BAC as part of that process.

Resolution of Legal and Ethical Issues in Relation to Ownership and Custody

- 13.7 Finally, we recommend that a dialogue be initiated with a view to achieve an early resolution of the legal and ethical questions in relationship to the ownership and custody rights to donated human tissue.