Yong Loo Lin School of Medicine
Centre for Biomedical Ethics

A Call for a More Holistic Approach to Governance of Biobanks – Experiences from Singapore

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Presentation overview

- What is the elusive whole?
  - Interface between Law and Ethics
- An Individual Altruistic Enterprise?
  - Informed Consent and its Challenges
  - Study on Banking of Surgical Residual Tissue
    - Realities of Informed Consent
  - Singapore's Legislation on Tissue Banking
- Biobanking as first and foremost a social enterprise
  - Solidarity; Equity; Sustainability
  - Shifting emphasis from regulation to partnership
  - Learning healthcare system and the context of ownership / stewardship

Scaling between Part and Whole

- "No property in the human body" rule (Williams v Williams)
- Some exceptions (Jocelyn Edwards [2011])
- Property is part of broader understanding of ownership
  - Property as a legal notion has been used as a device or tool (as means to an end), and as an anti-regulatory tool (Riles, 2004)
- Challenge: Constituting a "part" often depends on making explicit everything that is known about its circumstances (Strathern 2004)
- Ambiguity of context and processes

National University Health System Tissue Repository (NUHS TR)

- The NUHS Tissue Repository (NUHS TR) is a core facility located in the Department of Pathology at the National University Hospital (NUH).
- The purpose of the TR is to provide medical researchers at NUH and NUS with high quality clinical samples and data in a manner that is safe, ethical and efficient.
- NUHS Tissue Steering Committee review process for tissue requests and operations
- Requests for tissue must be approved by two different committees.
  - Ethics Committee or Institutional Review Board
  - Tissue Allocations Committee

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Various Types of Consent Model

Research ethics

Table 1 Overview of various forms of consent and the challenges they address

Type of consent	Description
Passive/tacit/silent consent	Presuming that the persons object if they do not consent.
Implicit consent/inferred consent	Consent is given implicitly in or can be inferred from an action. For example, a person consenting to cancer surgery implicitly consents to being cut in with a scalpel.
Presumed consent	Consent under the presumption that people (in general) would have consented to the treatment or research were they able to consent.
Hypothetical consent	Consent under the presumption that a person would have consented to the treatment or research were she or he able to consent.
Future/deferred consent	Postponing the consent procedure.
Broad consent/general consent/generic consent	Consenting to a wide (broadly specified) range of options.
Blanket consent/open consent	Consent to an unlimited range of options.

B. Hofmann J.Med.Ethics 2009;35;125-129; Prepared by Chan TW

NUH Study on Surgical Leftover Tissue

- Tissue Collection:
  - General Consent for Storage (De-identified Basis)
  - Specific Consent for Tissue Banking
- Using the empirical results collected by: Systematic literature review of 153 publications

  (Joanna Briggs Institute method of Comprehensive Systematic Review for evidence based healthcare –publications from 1990 to 2011)

Source: Chan TW, Mackey SJ, Hegney D, (2012) Patients' consent and donation of their residual biological samples: A systematic review. *International Journal of Evidence-Based Healthcare - International Journal of Evidence Based Healthcare* 2012; 10: 9-26.

- Quantitative analysis of consent collected at a national hospital

  (NUH, from 2002 to 2011, n = 167,329)
- Qualitative interviews of donors who had donated their HBMs

  (NUH, from 2011-2013, n = 100)

Source: Chan TW, Research Ethics and Consent on the Collection and Use of Human Biological Materials. NUS: May 2015

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Research findings

1. Patients' consent to the use of their left-over tissues are influenced by many and varied factors. Primarily these factors included: benefits to self and other and trust in research and researchers.
   Specific consent-taking was not of especial moral significance other than an expression of respect for persons.
2. Healthcare institutions and regulatory authorities must provide strict safeguards and controls in order to maintain privacy and confidentiality of the patients.
   Systemic safeguards were taken for granted and likely to have had a greater impact on decision to donate.
3. No clear understanding or concern for risks (except privacy & confidentiality). Most preferred tissue not to be wasted.
4. Patients have different views on the commercial use of their tissues.
   General equity concerns and reciprocity.

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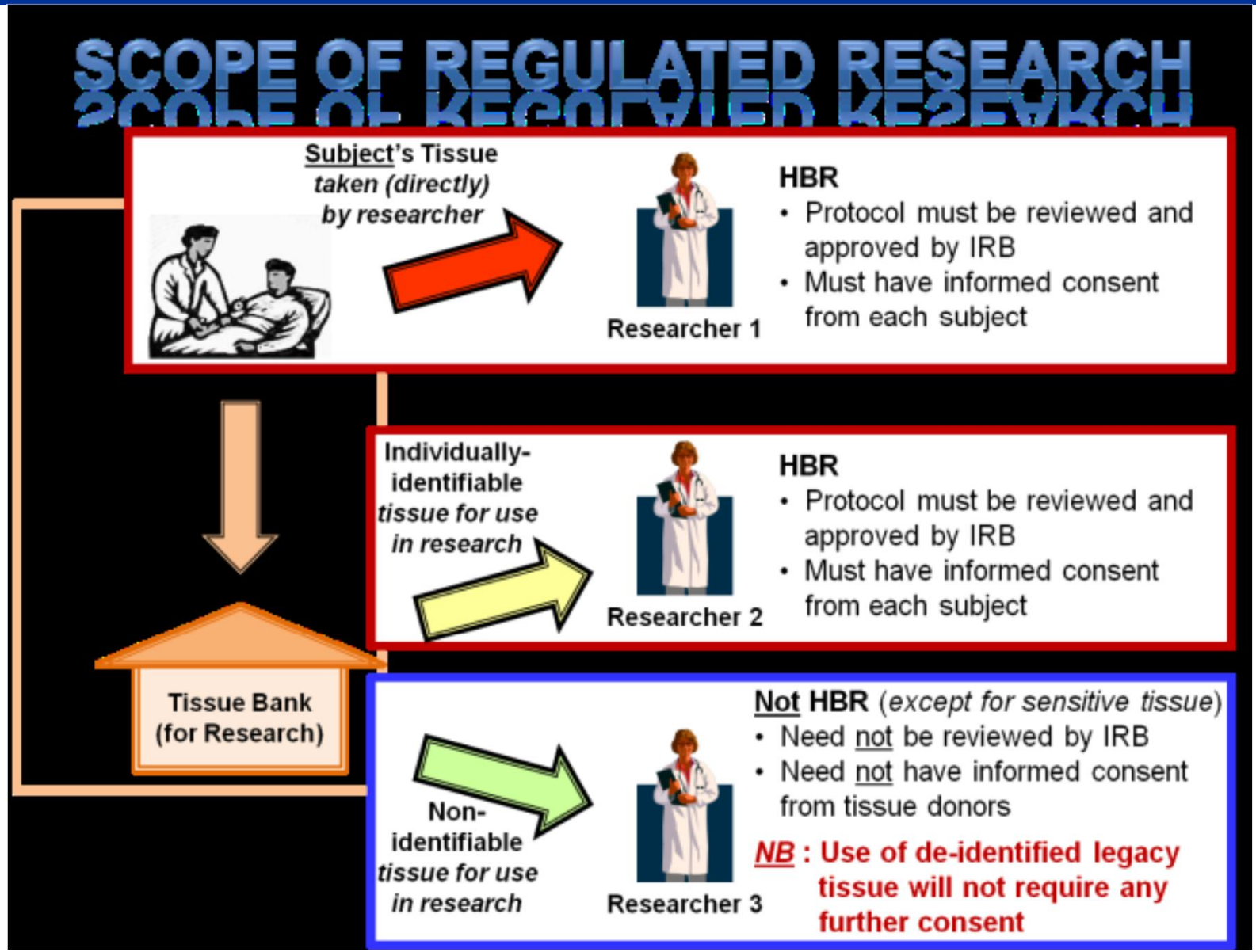
Human Biomedical Research Act – Tissue Regulation

- Protect Safety and Welfare of Tissue Donors.
- Prohibit commercial trading of human tissue.
- Ensure human tissue used in biomedical research are obtained only through altruistic donation.
- Provisions on Informed Consent:
  - Broad consent for generic research
  - Specific consent for sensitive or restricted research
  - Benefit outweighs Risk (especially for vulnerable participants)
  - Legacy tissue – no consent required if de-identified.

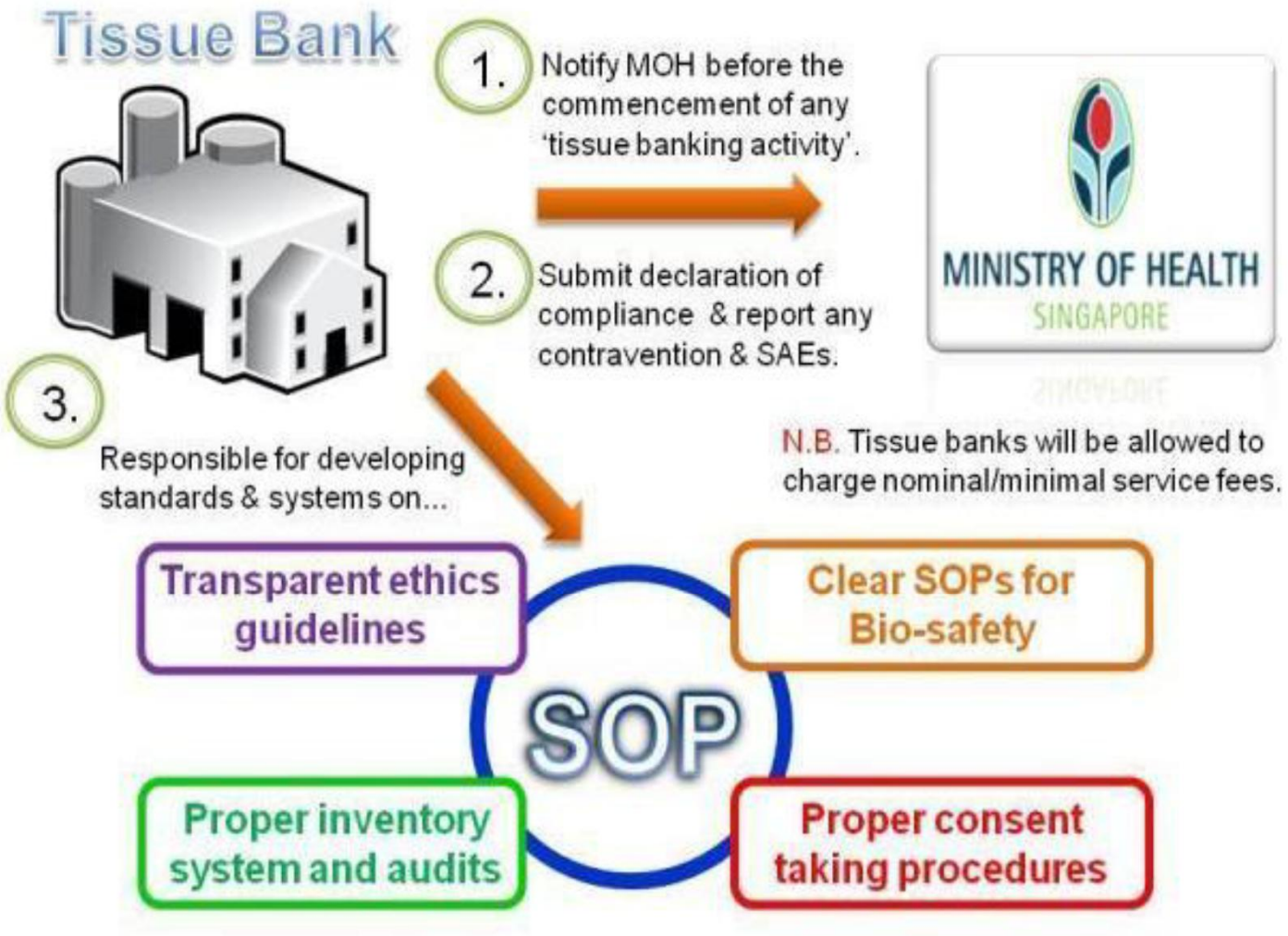
Regulated Tissue

- Tissue bank generally refers to an individual, an institution or an organisation that conducts tissue banking activities.
- Tissue banking activity means a structured and organised collection, by one or more individuals or a body of persons, whether corporate or unincorporate or other organisation, of tissues as a resource for the purposes of facilitating biomedical research or for public health or epidemiological purposes or any combination of such purposes.
- Exclusions:
  - Substantially manipulated tissue (but not cutting, grinding, centrifugation, vitrification, cryopreservation, freezing, etc.)
  - Hair shaft, nail plate, naturally excreted fluids and waste products.



Source: Ministry of Health, Singapore, November 2014

DUTIES AND RESPONSIBILITIES OF TISSUE BANK



Source: Ministry of Health, Singapore, November 2014

Provisions on Informed Consent

The person giving consent must first have been properly informed and provided with (at least) a prescribed list of information about the research. This prescribed list of information [in subsidiary legislation] will include essential information such as:

(a) the purpose of the tissue donation i.e. what the tissue may be used for;

(b) the foreseeable risks involved in the removal of the tissue;

(c) the voluntary nature of the tissue donation, and the donor's renunciation of any property rights to the donated tissue & any IP claims derived from the use of the tissue;

(d) the donor's right to withdraw consent, and the (limited) effects should consent be withdrawn i.e. withdrawal only effective if the tissue is still individually-identifiable, and will only be effective prospectively to prevent any further use;

(e) whether the donor will be informed of any incidental findings;

(f) whether the tissue will be used in an individually identifiable form;

(g) Whether whole genome sequencing will be done to the tissue in de-identified form.

Consent Focus

As a default position, the standard as to what constitutes "appropriate consent" is consent that is obtained:

1. before the tissue is removed from the donor.
2. in writing i.e. *written consent*;
3. from the donor personally i.e. *personal consent*;
4. after the donor has been given a full explanation on the nature of the tissue donation and the subsequent use of the tissue

Where tissue was removed from a donor for a therapeutic or diagnostic purpose, no person is allowed to:

a. Store the tissue for use other than the intended therapeutic or diagnostic purpose;
b. Supply the tissue for use in research; or
c. Use the tissue in research, unless there is prior consent to do so. No tissue should be used for any purpose other than what it was consented to be used for.

HBR Act – Additional Features

- Detailed list of informational requirements set out in the legislation, including investigational nature and purpose of research, and reasonably foreseeable risks.
- Note conditions for waiver of appropriate consent by IRB
  - Minimal risk
  - Situational necessity
  - Importance of research / social value
- Withdrawal of consent

KEY CONTROLLING PROVISIONS

-Consent requirements-

Consent for tissues to be used in individually-identifiable form

- *Donors can choose to decline allowing their tissues to be made available for research in individually-identifiable form*

POSSIBLE MODULAR CONSENT FORM TEMPLATE (see handout)

SECTION B : SPECIFIC OPT-OUT SECTIONS

		Agree	Disagree
1.	In the event that research on my biospecimens show that clinical intervention, if provided, can prevent further deterioration of any disease suspected or diagnosed, I give permission to be identified and contacted for the purpose of clinical intervention. ("I understand that where possible, I would be contacted by my care provider or the healthcare institution to which I have an on-going relationship. If I am the research subject, the person contacting me would likely be the Principal Investigator or the one who initiated my recruitment into the project.)	☐	☐
2.	I consent to my donated biospecimens being used in an individually-identifiable form for research.	☐	☐

I _____ (NRIC No _____) agree to only the ticked boxes that I have given consent for in the above Opt-Out sections.

Consent form can be 'tiered' with specific opt-out sections so that donors can, at the point of donation, either agree or disagree to the use of their tissues in individually-identifiable form. If they had agreed to all the items for General Consent, they could proceed to donate their tissues, even if they choose to disagree with the specific opt-out sections in Section B (above).

Other Protected Interests

- Protection of Confidentiality and Privacy of Donor: Any person having custody or control of human tissue must exercise all reasonable care to protect any individually-identifiable information concerning the tissue donors against :
  a) any accidental or unlawful loss, modification, destruction; or
  b) any unauthorised access, modification, disclosure or use.
- Sensitive tissues: The taking of sensitive tissues (gametes & embryos) for research requires personal consent to be obtained. Therefore, such sensitive tissues cannot be taken from persons who are unable to give personal consent (e.g. mentally incapacitated adults and minors without understanding). Sensitive legacy tissues (whether in de-identified or anonymised form or identifiable form) cannot be used without personal consent.

Duties & Responsibilities

A Tissue Bank must:

1. Notify MOH before the commencement of the first tissue banking activity.
2. Submit a declaration of compliance at the onset and thereafter, at least annually, for all tissue banking activity conducted by the Tissue Bank.
3. Report to MOH any information that it becomes aware of regarding :
   a. the (suspected) commission of any contravention under the HBR Act;
   b. the occurrence of any serious adverse events associated with the use of any tissue from the bank; and any other matters as may be required by MOH.
4. Develop internal policies, standards and systems for the proper conduct of its tissue banking operation, including :
   a. clear and transparent ethical guidelines and policies;
   b. clear SOPs to ensure integrity and biological safety of tissue holdings;
   c. proper inventory system with periodic audits;
   d. clear procedures and documentation for consent-taking.

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Non-commercialisation

- Tissue banks are not allowed to sell or trade any tissue samples they have acquired. However, tissue banks will be allowed to charge nominal/minimal service fees (i.e. cost recovery) for the storage and processing of tissues. Tissue banks will have to substantiate the fees charged.
- Release of de-identified legacy tissue (taken without consent) for research: Tissue banks must sight expert committee reviews for scientific merit of the research before releasing the tissues.

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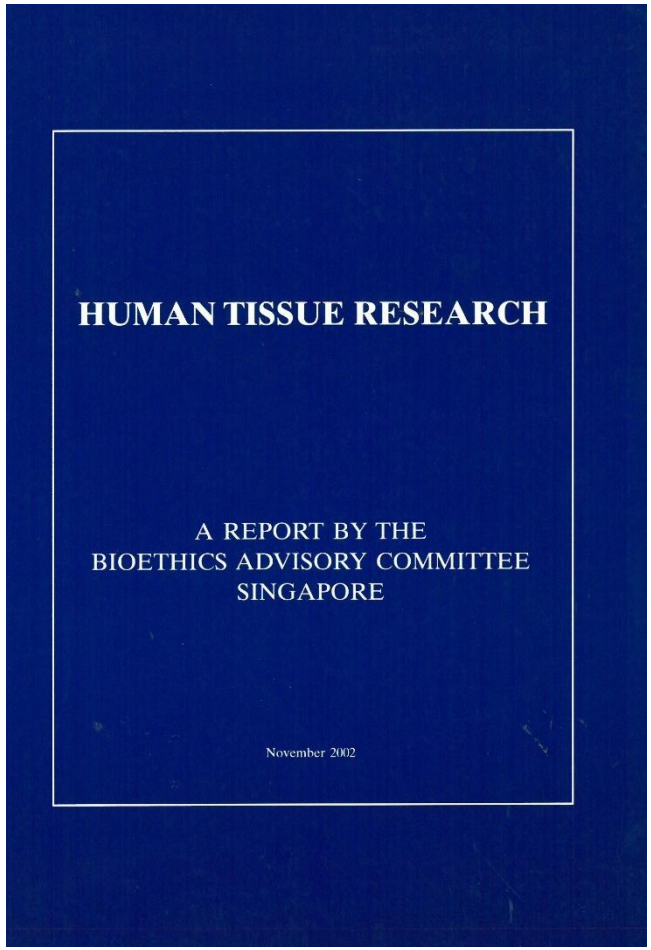
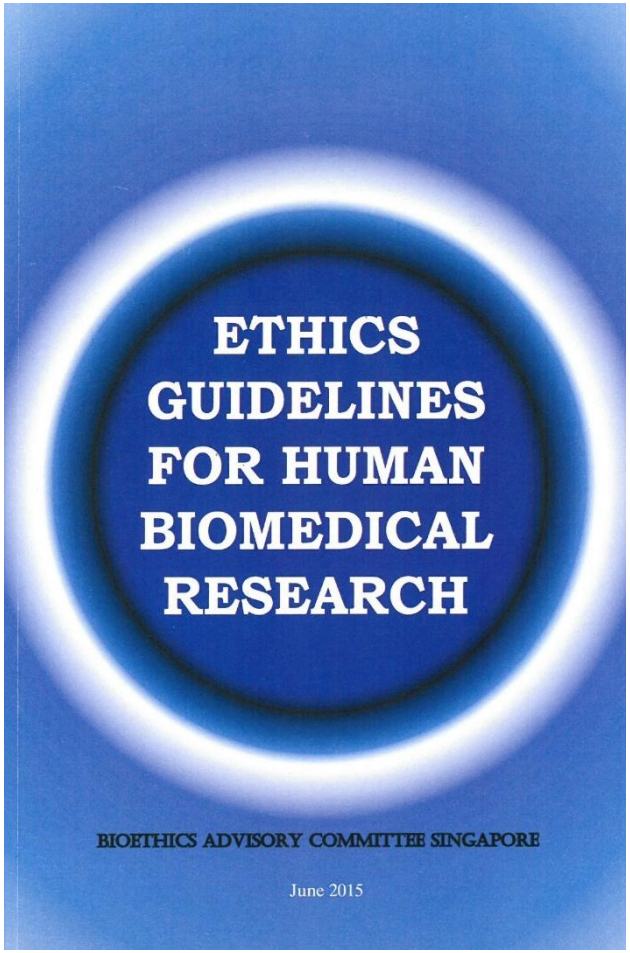
Broader Ethical Context





BAC's Ethical Principles

Five ethical principles set of by the BAC (2015) as:

Respect for persons
Safeguard welfare, especially of vulnerable subjects

Solidarity (Reciprocity)
Balance between public interests and individual rights

Proportionality
Regulation of research in proportion to risk

Justice
Equitably sharing of benefit and burden

Sustainability
Research process and outcome sustainable; will not jeopardise or prejudice the welfare of later generations

Ø Other considerations: Beneficence and Research Integrity

Solidarity

(UK Nuffield Council on Bioethics, 2011)

- Signifying shared practices reflecting a collective commitment to carry 'costs' (financial, social, emotional or otherwise) to assist others.
- Three tiers by which it is practiced:
  - Inter-personal
  - Group practices (e.g. good or best practices)
  - Contractual or legal (most formal)
- Different from requirements of justice, as fairness for instance.

Shift in Value Emphasis?

Shift from a “regulatory” model to a “partnership” model

- Regulatory model – IRBs or RECs review protocols based on guidelines as a series of minimum ethical standards.
- Focus on regulation, standards and compliance in order to prevent research participants from being exploited.
- Partnership model – actively involves all parties with a focus on providing positive benefits to society

Source: DW Dowdy. Partnership as an ethical model for medical research in developing countries. Journal of medical ethics (2006) 32:357-360

Learning Healthcare System Ethics Framework – 7 Fundamental Obligations:

- Respect for rights and dignity of patients
- Address health inequalities
- Conduct continuous learning activities that improve quality of clinical care and health care systems
- Contribute to the common purpose of improving quality and value of clinical care and health care systems

Source: RR Faden, NE Kass, SN Goodman, P Pronovost, S Tunis, TL Beachamp. An Ethics Framework for a Learning Health Care System. Hastings Center Report 2013:S16-S27.

Shift in Value Emphasis? (1)

- What is the appropriate role of individual participants? And what are their entitlements?
  - Contractarian or Partnership?
  - The Place of Public Participation and Deliberation?
- Is there a need for leadership/accountability over the issues?

  Should there be an allocative role, with a re-distributive function? (Gostin, 2014)
- Shift from a "regulatory" model to a "partnership" model
  - Regulatory model – IRBs or RECs review protocols based on guidelines as a series of minimum ethical standards.
  - Focus on regulation, standards and compliance in order to prevent research participants from being exploited.
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Shift in Value Emphasis? (2)

- Learning Healthcare System Ethics Framework – Fundamental Obligations include:
  - Respect for rights and dignity of patients
  - Address health inequalities
  - Conduct continuous learning activities that improve quality of clinical care and health care systems
  - Contribute to the common purpose of improving quality and value of clinical care and health care systems

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- Revisiting ownership (as stewardship?) and what is being owned (Strathern 2004)

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