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Guideline on the Use of Human Biological Tissues for Research

PREAMBLE

Human biological tissues or organs, removed in the course of medical procedures / treatment or excess samples left over after diagnostic investigations, are rich resources for immediate or future research.

Generally, patients undergoing surgery do not have their consent obtained nor are informed regarding the further use or handling of their biological materials. To protect the rights and fundamental freedom of these patients and in view of the increasing flow of biological materials across countries and borders, there is a need to standardize practices amongst the various Institutional Review Board / Independent Ethics Committee (IRB / IEC) and institutions in the country in the collection, storage and use of such materials for research. Clear guidelines must be established particularly on the principle of requesting consent, be it at the time of collection of the materials or after, and the introduction of a layered consent. This is extremely important as more researchers and institutions are capitalizing on the vast research potential of human tissues made available through routine medical procedures and investigations.

This guideline aims to draw attention to important ethical issues that should be considered when:

1. Conducting research on stored/archived human biological tissues which **had been collected** during routine investigation/treatment

2. Collecting biological tissues from patients undergoing routine investigation and treatment which **may be used** for future research, and

3. Conducting research involving **planned prospective collection** of human tissues including those for the purpose of bio-banking

This guideline is not intended to cover the use of such biological tissues for medical diagnostic purposes, disease surveillance or teaching.

It serves to advise the IRB / IEC on the general principles and approaches to address issues on using human biological tissues for research. While the IRB / IEC is expected to comply with this general guideline, there may be a need for adaptations to suit the individual institutions' environment and/or the requirements of a particular study.

The following ethical principles form the basis for the formulation of this guideline:

- beneficence (doing good)
- non-maleficence (preventing or mitigating harm)
- fidelity and trust within the investigator/participant relationship
- personal dignity of study participants or subjects

- autonomy pertaining to both informed, voluntary, competent decision making (informed consent) and
- privacy of personal information

1. CONDUCTING RESEARCH ON STORED / ARCHIVED HUMAN BIOLOGICAL TISSUES WHICH HAD BEEN COLLECTED DURING ROUTINE INVESTIGATION / TREATMENT

The key issues to be considered include:

- Confidentiality
- IRB / IEC Approval

1.1 Confidentiality

It is acceptable to use archived or surplus human materials collected during routine surgical treatment or medical diagnosis for research without the need for individual written consent provided the samples are anonymized and not possible to be linked to identifiable individuals / data.

1.2 IRB / IEC Approval

IRB / IEC approval must be obtained before these tissues are used for research.

2. COLLECTING BIOLOGICAL TISSUES FROM PATIENTS UNDERGOING ROUTINE INVESTIGATION AND TREATMENT WHICH MAY BE USED FOR FUTURE RESEARCH

The key issues to be considered include:

- Informed consent
- Confidentiality
- Custodianship and Access
- Standards
- IRB / IEC Approval

2.1 Informed Consent

There must be explicit separation of consent to surgery, or other forms of treatment / procedure from consent to use the tissues or tissues surplus for research.

Informed consent for collection of human biological tissues for research can be taken before or after the surgery/procedure. However, it is important that such consent should not in anyway distract the patient/subject or cause anxiety to him/her in giving consent for the surgery/procedure which should take precedence over consent for research. It should be made clear to patients or subjects that the consent is voluntary and can be withdrawn at any time and this will not affect their treatment in any way.

Requesting consent for collecting tissues from subjects before surgery or procedure is permissible if there is requirement for special procedures to be adhered to in the collection, handling and preservation of the tissues.

In cases of children and/or other vulnerable groups consent should be obtained from the legal guardian or next-of-kin.

2.2 Confidentiality

Refer to 3.2.

2.3 Custodian and Access

From a legal perspective, tissues or organs removed from surgery might be considered to be “abandoned” by the patient and can be used in ways seen fit by the institution.

Samples of tissues collected from the patients or subjects are considered as “gifts” or “donations” although it is conditional in that research conducted is according to ethical standards.

2.4 Standards

Refer to 3.4.

2.5 IRB / IEC Approval

Although consent from patient/subjects has been obtained for the use of the tissues in future research, approval from IRB / IEC must first be obtained for each subsequent study.

3. CONDUCTING RESEARCH INVOLVING PROSPECTIVE COLLECTION OF HUMAN TISSUES INCLUDING THOSE FOR THE PURPOSE OF BIO-BANKING

The key issues to be considered in prospective collection of human biological tissues include:

- Informed Consent
- Confidentiality
- Custodianship and Access
- Standards
- Feedback of Research Information
- IRB / IEC Approval

3.1 Informed Consent

In research which has been planned to include collection of human biological tissues, approval from the IRB/IEC and informed consent from the participating subjects must be obtained prior to the commencement of the study.

Should the researcher plan to store and use the tissues for future research/studies, a multi-layered consent should be obtained. A separate informed consent for each request should be obtained from the subject. The request for consent may include:

- Consent to the specific experiment(s) already planned
- Consent for storage and future use
- Consent for access to medical records and information
- Consent for re-contacting the subject for more data

Generic consent to use the tissues for future research without conditions is not permissible.

Subjects should be informed about the future research when it is finally carried out, whenever practicable.

Consent from children, the elderly, disabled and other vulnerable groups should be obtained as prescribed in the Good Clinical Practice guidelines (Malaysian Guidelines for Good Clinical Practice, 2004).

In the information sheet for the primary/main study for which approval of IRB / IEC is requested, researchers must provide potential study subjects the following information:

- Purpose of the research
- Possible future research including type of studies, type of diseases that could be investigated, possible impact of research and benefits
- Type and amount of tissue to be taken (as well as location)
- The manner in which tissue will be taken, the safety & invasiveness of acquisition, the duration and conditions of preservation
- The potential uses for the tissue including any commercial uses
- The safeguards to protect the individual's privacy and confidentiality
- Identifying information attached to specific tissue, and its traceability
- How the use of the tissue could affect privacy
- The right to withdraw and arrangement for disposal of tissues and data

3.2 Confidentiality

Personal data and information may prejudice participants against health insurance and employment. Hence, personal identifiers should be removed as far and as early as possible (anonymizations) so that it is not possible to link the results of the tests to identifiable individuals. The level and process of anonymisation is to be approved by the IRB / IEC.

There must be a clear and stringent privacy framework so that data are protected.

There should be restricted access to data and if necessary, a third party (independent body) may be used to re-link results with personal data which may provide some benefit to the patient or to the community (e.g. relate prognosis or outcome to clinical data). This should be done within the confines of strict ethical guidelines.

The key principles on personal information are:

- Personal information must be treated as confidential
- All medical research using identifiable personal information must be approved by an IRB / IEC
- All personal information must be coded or anonymized as far and as early as possible in the data processing

- Principal investigators are responsible for ensuring that procedures and security arrangements are sufficient to prevent breaches of confidentiality
- Researchers must decide which information or results will be made available to the people involved

3.3 Custodianship and Access

Once a sample has been obtained from a patient or subject, the appropriate custodian of the sample is the institution that collects the samples. The custodian therefore retains the responsibility to protect and regulate the use, storage, access, transfer and disposal of the tissues.

Patients are informed that their donated tissue or product derived from it may be used for commercial purpose and that they will not be entitled to a share of any profits that might ensue.

Intellectual property arising from the research belongs to the researchers and the institution.

Tissues samples donated by a patient must not be used for financial gain or sold to a third party.

Any request for access to the human biological tissues must be approved by a committee following a set of criteria agreed to by the institution or custodian.

Custodians must ensure that any use of the tissue samples for research must have prior IRB / IEC approval.

3.4 Standards

Human biological tissues collected for research must be kept and handled according to specified biobanking standards. It is unethical to collect and process specimens without regards to proper standards because it may impact on the reliability and validity of the tests performed and consequently the research findings.

Issues of varied biobanking standards and varied quality of specimens remain relevant and important concerns in research employing new technologies such as micro-array and proteomics. To ensure compliance, a set of Standard Operating Procedures for samples acquisition, transport, processing, archiving, disposal, safety should be made available.

3.5 Feedback of Research Information

A participant of research has the right to know his/her results of tests conducted in the research which may have a bearing on his/her health. He/She may however choose not to exercise this right.

The researcher should make public the general results (not individual) of the research in a medium which is easily accessible by the general public.

Researchers should decide at the beginning on the type of information that will be made available to the patients and/or the community and this should be indicated in the submission to the IRB / IEC.

IRB / IEC Approval

All research involving human subjects and/or collection of human biological tissues must obtain approval from the IRB / IEC.

Despite IRB / IEC approval for use of human biological tissues for future research, the researchers must obtain new approval for specified projects utilizing these tissues.

In the case of anonymized research, the level and process of anonymization shall be confirmed by a review procedure approved by the IRB / IEC.

DEFINITIONS

Tissue	A collection of human cells with or without the intercellular substances surrounding them (these include blood, hair, nails, etc.)
Custodian	Any person who is responsible for collection, storage, and/or regulating access to human tissues for research purposes
Anonymized tissues	Tissues where the link between the specimen and the identity of the donor has been removed
Tissue bank	Any collection of human tissues which are being stored for planned or unplanned future research

REFERENCES

1. Human tissue and biological samples for use in research: Operational and ethical guidelines Human Tissue and Biological Samples for use in Research. Operational and Ethical Guidelines. Medical Research Council, 2001.

2. MRC Operational and Ethical Guidelines. Clarification following passage of the Human Tissue Act 2004, 2005.

3. Nuffield Council on Bioethics Report: "Human Tissue: Ethical and Legal issues", 1995.

4. Trouet C (2004) New European guidelines for the use of stored human biological materials in biomedical research. J Med Ethics, 30, 99-103.

5. Garrath W (2005) Bioethics and large-scale biobanking: Individualistic ethics and collective projects. Genomics, Society and Policy, 1, 50-66.

6. Malaysian Guidelines for Good Clinical Practice, 2nd edition, 2004.