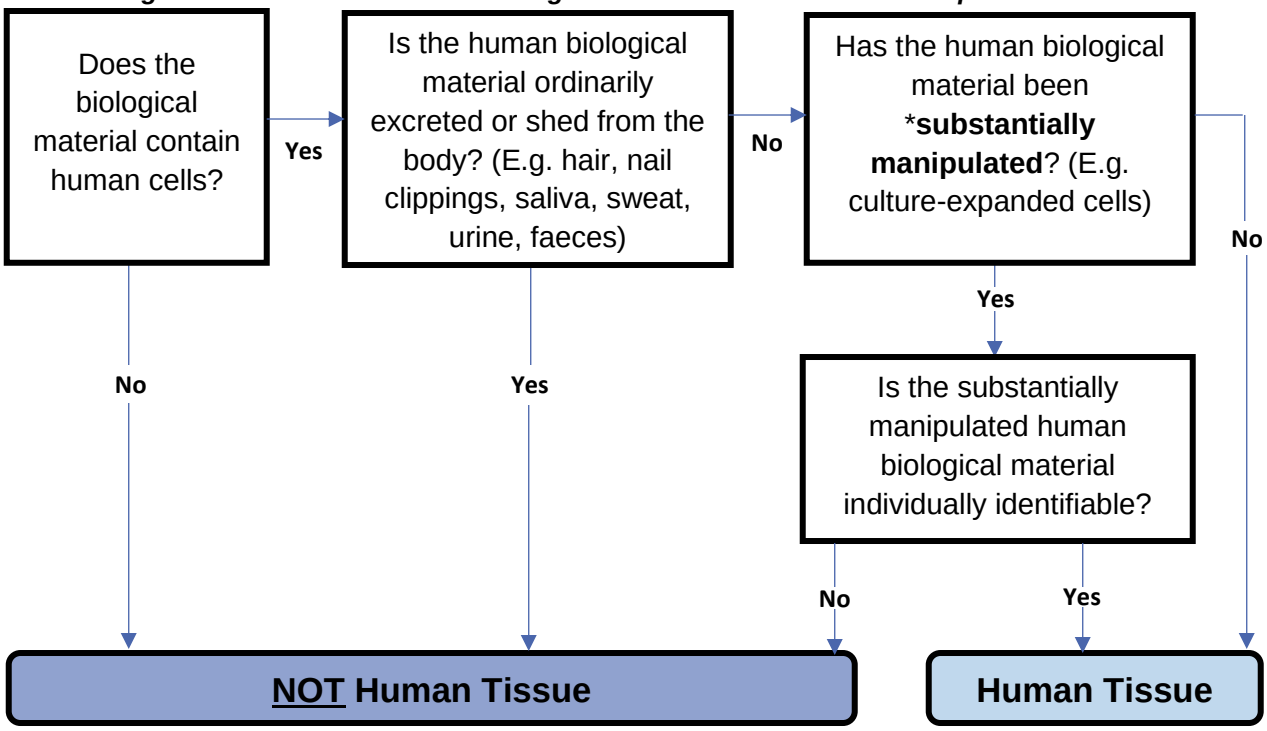
CHAPTER 9

TISSUE BANKS

9.1 Definition of Human Tissue, Tissue Bank and Tissue Banking Activities

The Human Biomedical Research Act (HBRA) 2015 defines **Human Tissue (HT)** as any biological material obtained from the human body that consists of, or includes, human cells but excludes human biological material specified in the First Schedule of the HBRA. This is summarized in **Figure 9**.

Figure 9: Schematic chart outlining the definition of human tissue per the HBRA.



*A sample is considered to be substantially manipulated if it has been processed in a manner such that its functional, structural and biological characteristics are substantially manipulated as compared to the time of collection from the donor. Processes that would not be considered to be substantial manipulation include cutting, grinding, shaping, centrifugation, soaking in antibiotic or antimicrobial solutions, sterilization, low-level irradiation, cell separation, concentration or purification, filtering, lyophilisation, freezing, cryopreservation, vitrification.

A **Tissue Bank (TB)** refers to an individual or a body of persons, whether corporate or unincorporate, or other organisation, that carries on or conducts any tissue banking activity.

However, tissue banking activities which is solely for the purpose of the person's or organization's own research, which falls within any of the following descriptions, would not be considered a TB:

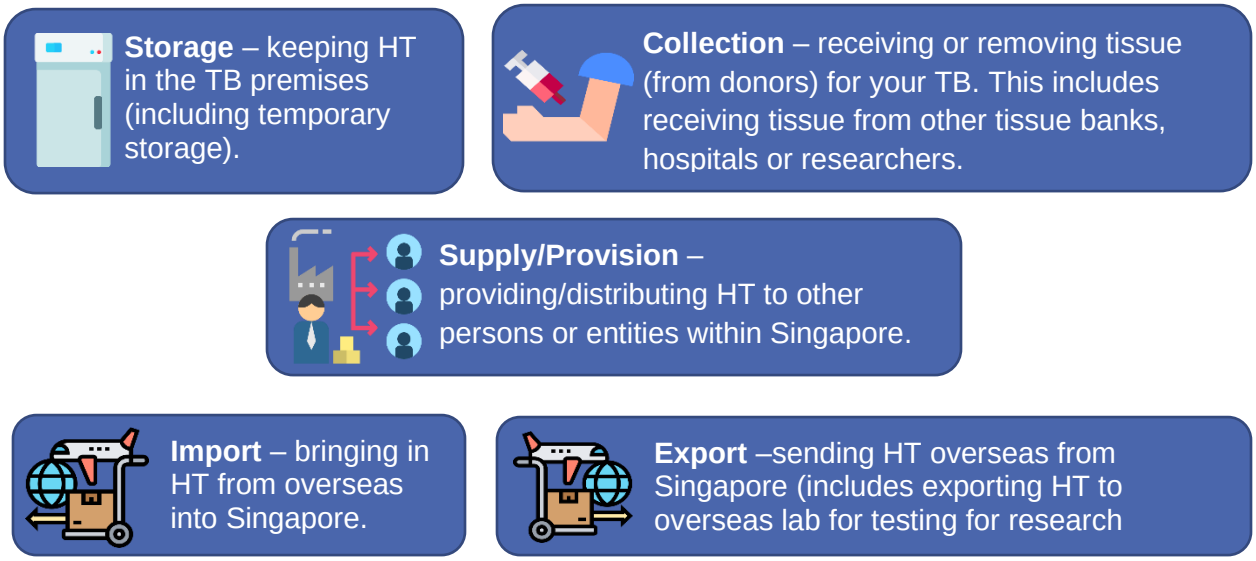
a. National public health research as defined in and conducted in accordance with section 59A of the Infectious Diseases Act (Cap. 137);

b. Clinical trials (CT) of health products conducted in accordance with the Health Products Act (Cap. 122D);

c. Clinical trials of medicinal products conducted in accordance with the Medicines Act (Cap. 176);

d. Human Biomedical Research (HBR) regulated under the HBRA (HBRA Section 37 - Restrictions on activities relating to human tissue, will still apply).

Tissue banking activity refers to a structured and an organized activity involving human tissue for the purposes of facilitating current or future research or for public health or epidemiological purposes or any combination of such purposes including any of the following activities:



Despite the above paragraph, tissue banking activities exclude the following:

a. Institution-based central laboratories that are set up for the primary purposes of clinical diagnosis or therapeutic treatment and not conducting tissue banking activities as described above.
b. Tissue banking activities as part of contracted duties solely to support a clinical trial or HBR (e.g. Contract Research Organisations (CROs), processing laboratories).

9.2 Tissue Bank Registration

With the activation of the HBRA Human Tissue Framework (HTF) on 01 November 2019, researchers who are collecting, storing, importing, supplying or exporting human tissue would need to do so under the supervision and control of a tissue bank. Some common examples of tissue banking activities that require tissue bank / tissue collection registration include:

a) Collection of additional tissue on top of what is required for the primary scope of the current research study solely for storage and use in future research (i.e., study not yet approved by an IRB).

b) Collection of tissue solely for bio-banking (where tissue is not collected for a research study that requires/ had obtained IRB approval).

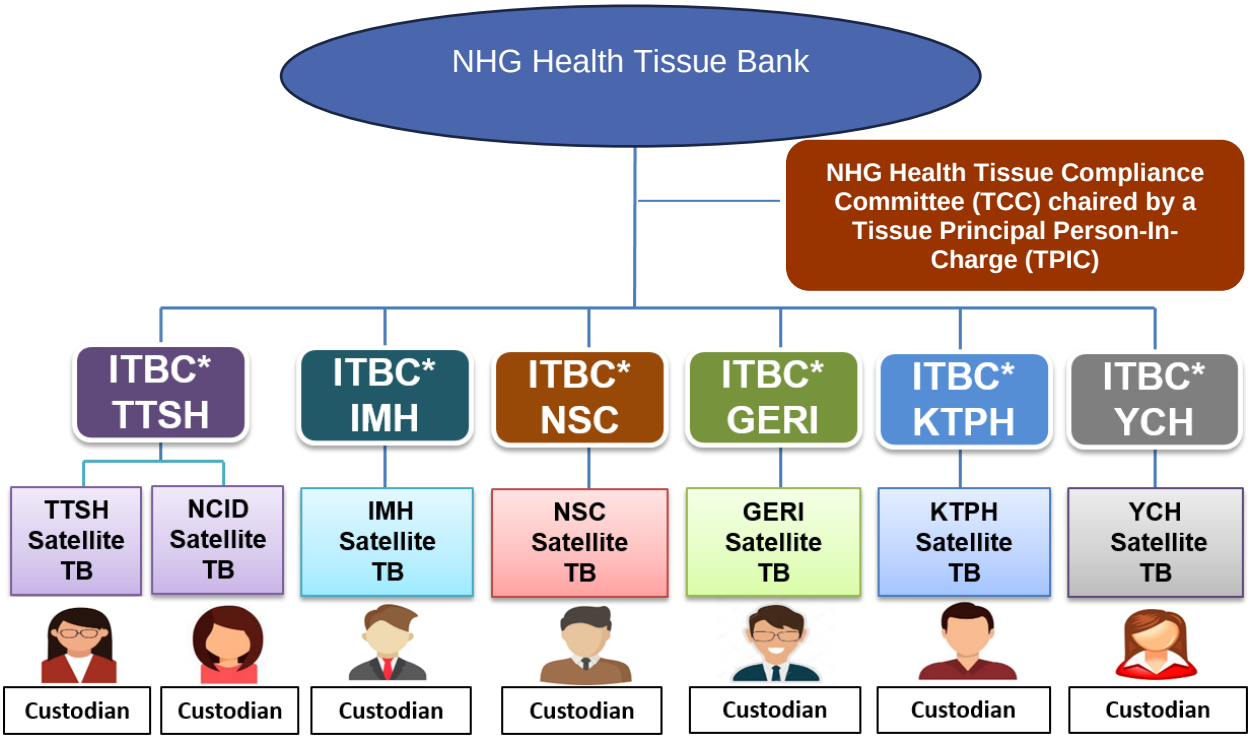
c) Storage of leftover tissue from completed studies for use in future research.

d) Supply of leftover tissue from completed studies to another IRB approved research (HBR or clinical trial) where the researcher is not a PI, Co-I or collaborator.

For NHG Health researchers, the tissue bank / tissue collection application process is described in **Section 9.2.1 and 9.2.2**. Researchers from non-NHG institutions should check with their respective institution research office on the tissue bank registration process if they are performing any of the above activities.

9.2.1 NHG Health Tissue Governance Structure

Figure 10: NHG Health Tissue Governance Structure



NHG Health has adopted a mothership model with multiple satellite tissue banks under its supervision as illustrated in **Figure 10** and has declared itself as one tissue bank to the Ministry of Health (MOH).

9.2.1.1 Responsibilities of NHG Health Tissue Compliance Committee (TCC)

All NHG Health institutional tissue banks are governed under the oversight of the NHG Health Tissue Compliance Committee. Responsibilities of the NHG Health TCC include:

a. Formulating and maintaining tissue bank policies and SOPs

b. Reviewing and approving Tissue Bank / Tissue Collection applications

c. Conducting continuing review of ongoing tissue banks and tissue collection protocols annually

d. Reviewing non-compliance reports, Serious Adverse Event (SAE) reports, Untoward Occurrence (UO) reports submitted by the Custodian / Tissue Collection Applicant (TCA).

e. Monitoring Tissue Banking Activities in NHG Health

9.2.1.2 Responsibilities of Tissue Principal Person-In-Charge (TPIC)

The NHG Health TCC is chaired by the TPIC. On behalf of the NHG Health Tissue Bank, the TPIC performs the following functions:

a. Notifies MOH before the commencement of any tissue banking activity conducted under the supervision of the NHG Health Tissue Bank.

b. Reports any suspected offence or contravention to the legal provisions set out in the HBRA and its Regulations.

c. Reports any Serious Adverse Event (SAE) resulting from tissue banking activity (intended for human application) conducted under the supervision of the NHG Health Tissue Bank.

d. Reports any Untoward Occurrence (UO) resulting from the removal of human tissue conducted under the supervision of the NHG Health Tissue Bank.

e. Submits a Declaration of Compliance to MOH annually.

9.2.1.3 Responsibilities of Institutional Tissue Bank Committee (ITBC)

The ITBC is an institution-endorsed committee, which comprises clinician(s) practicing in the institution, researcher(s) and Institution Representative for Research (IR). The ITBC endorses tissue bank and tissue collection applications and reviews requests for the utilization of tissue stored in the institution's tissue banks.

Researchers from non-NHG institutions should check with their respective institution research office on the tissue bank governance structure.

9.2.2 NHG Health Tissue Bank / Tissue Collection Application Process

Researchers from NHG Health institutions may appoint a tissue bank custodian who bears the overall responsibility for the set up and maintenance of the tissue banks. The NHG Health

custodian / tissue collection applicant (TCA) should download the tissue bank / tissue collection application form(s) from the NHG Health Research Website, complete them, and obtain endorsement from the Department Representative (DR) and Institutional Tissue Bank Committee (ITBC) before submitting the form(s) to the NHG Health Tissue Compliance Committee (TCC) Secretariat via NHGTCCSecretariat@nhg.com.sg. The TCC Secretariat would perform a preliminary review of the applications and route them to the DSRB / TCC for review.

For biobank tissue collections independent from an IRB approved study or researchers who are collecting extra tissue for future research, both the tissue bank application form and the tissue collection application form would need to be completed. The tissue collection application form would be additionally reviewed and acknowledged by the DSRB before it is routed to the TCC for review and approval. This is to ensure that the recruitment and consent process for donors comply with the ethics requirements and the HBRA.

For researchers who intend to store leftover tissue from completed studies for future research that has not been approved by an IRB or intend to supply the leftover tissue to another IRB approved research (HBR or clinical trial) where he/she is not a PI, Co-I or collaborator, only the tissue bank application form would need to be completed. The endorsed tissue bank application form would be routed by the TCC Secretariat to the TCC for approval. DSRB review would not be required in such instances as these completed studies had previously been approved by the IRB and do not involve new tissue collections.

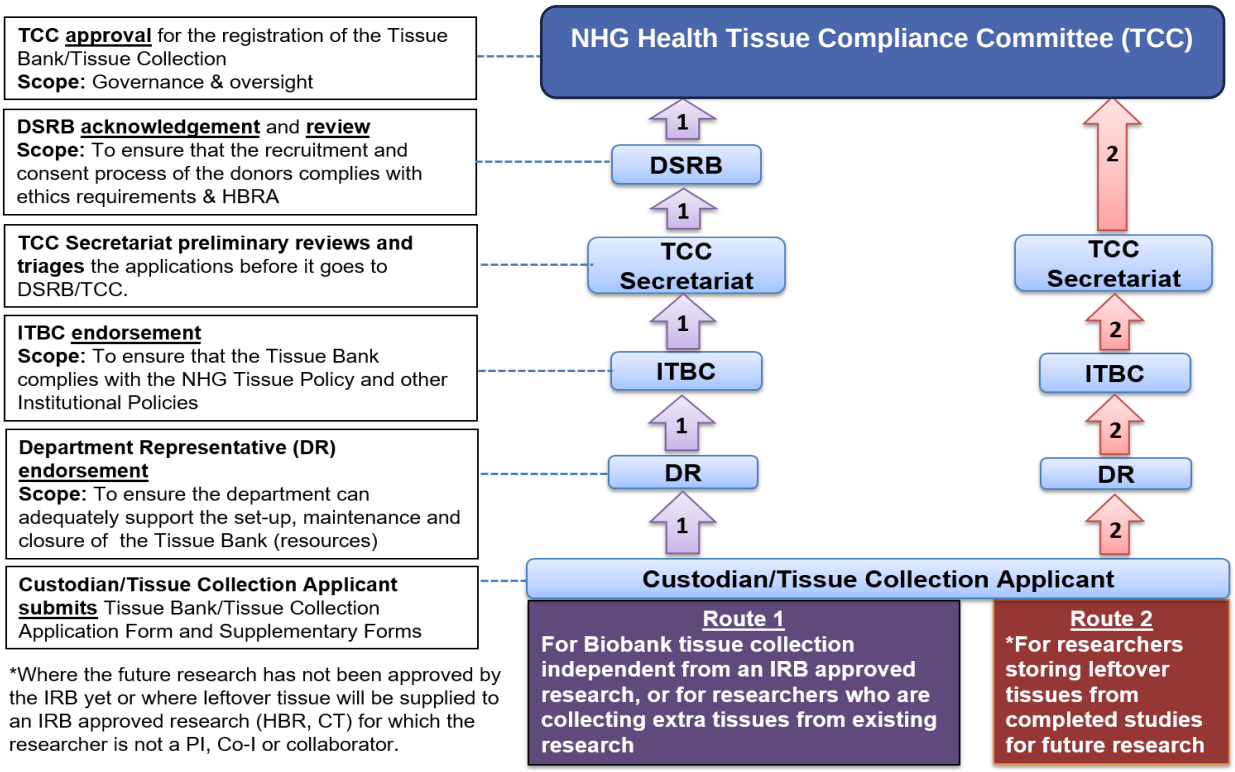
The NHG Health tissue bank / tissue collection registration process is summarized in **Figure 11**.

Quick Tip

Confused over which form to submit? (i.e., tissue bank application form, tissue collection form or both?) The Tissue Bank Application form contains a guide that helps you to determine the correct form to use.

NOTE: The tissue bank / tissue collection application forms can only be accessed when you have direct access to the NHG Health Intranet. These documents are strictly for internal circulation among NHG Health Staff and Authorized personnel only.

Figure 11: NHG Health tissue bank / tissue collection application process.



9.2.3 NHG Health Tissue Bank / Tissue Collection Endorsement Process for Multi-site Collaborations

Tissue banks that straddle across more than one NHG institution

The custodian or TCA from all involved institutions will be required to submit an application to TCC. The application will need to first route to each of the institutions' DRs and ITBCs or equivalent for endorsements. This will allow all institutions to have oversight of the tissue banking activity. A lead tissue bank custodian may be identified to coordinate the applications.

Tissue Banks that straddle across NHG Health and non-NHG institutions and where a NHG Health institution is the Lead Tissue Bank

Regardless of the site of the tissue bank, the NHG Health custodian / TCA will be required to submit an application to TCC. The application should be endorsed by the NHG Health institution(s) DRs, ITBCs and CMBs or equivalent. CMB's acknowledgement is needed given the additional responsibilities that the NHG institution has to undertake as the lead tissue bank.

Tissue Banks that straddle across NHG Health and non-NHG institutions and where a non-NHG institution is the Lead Tissue Bank

Regardless of the site of the tissue bank, the NHG Health custodian / TCA will be required to submit an application to TCC. The endorsement of the NHG Health institution(s) HODs, ITBCs or equivalent are necessary. CMB endorsement is not required.

9.3 Key Human Tissue Framework Requirements

It is important to ensure that the tissue bank processes and documentation are aligned with the regulatory requirements of the HTF. Key HTF requirements for researchers to take note of include:

a) Operational requirements for collection, storage, supply, import and export of tissue for research

b) Consent requirements

c) Operational requirements for tissue banks that stores or supplies tissues for use in research involving human tissue transplantation

9.3.1 Key HTF Requirements for Tissue Banking Activities

9.3.1.1 Removal and Collection of Human Tissue

a) Appropriate consent must be obtained from the donor or donor's legal representative (where applicable) before the removal of tissue.

b) Human tissue should not be removed from any of the following persons unless the removal of the tissue was primarily for a therapeutic or diagnostic purpose:

   i) Adult or minor who lacks mental capacity;
   ii) Minor who lacks sufficient understanding and intelligence to give consent

   However, an IRB may waive the above requirement if the board is satisfied that
   i) The removal involves no more than minimal risk to that person; and
   ii) There are reasonable grounds to believe that the proposed areas of research cannot be carried out without the use of the tissue from the class of persons involved.

c) If the human tissue was removed from a donor for a therapeutic or diagnostic purpose, the tissue should not be stored, supplied or used for research or any other purpose unless the medical practitioner or healthcare institution had completed all necessary therapeutic or diagnostic procedures and no longer require the tissue or part of the tissue for the treatment. The medical practitioner should also document that a formal assessment had been performed to confirm that all therapeutic or diagnostic procedures have been

completed and the leftover tissue is no longer required for the patient's treatment, before it is used for research.

d) Personnel involved in tissue removal must be qualified and trained to do so.

e) Appropriate measures must be in place to prevent or control the spread of any communicable disease which is or may be due to the contamination or infection of any tissue.

f) Instruments and equipment used for the removal of tissue must undergo regular maintenance and subjected to quality controls.

g) An incidental finding (IF) policy on whether or not the tissue donor should be re-identified and informed in the case of an incidental finding in relation to a tissue should be formulated. The policy must be communicated to all donors and recipients of every tissue received by the tissue bank on or after 01 Nov 2019 (HTF activation date). If the policy provides for the donor to be re-identified and informed in the case of an IF, the donors' wishes should be communicated to the recipient as well.

9.3.1.2. Storage of Human Tissue

a) Appropriate consent must be obtained from the donor or donor's legal representative (where applicable) for the storage and subsequent use of tissue for future research.

b) The storage and/or subsequent use is in accordance with any conditions or restrictions specified as part of the appropriate consent

c) Measures must be in place to protect the confidentiality and maintain the privacy of information relating to the donor of each tissue.

9.3.1.3 Supply of Human Tissue

a) Human tissue may be supplied for use in research only after:
   i) Appropriate consent had been obtained for the tissue to be used in research;
   ii) The intended use is in accordance with any conditions or restrictions specified as part of the appropriate consent; and
   iii) The recipient is informed of the requirements referred to in (i) and (ii)

b) Before supplying individually-identifiable tissue for use in research, the tissue bank must ensure that:
   i) An institutional review board (IRB) has approved the proposed research that the tissue would be used for; and
   ii) There is documentary evidence provided by the receiving party that the receiving party will ensure that the intended use of the tissue is in accordance with any restrictions/conditions of the donors' appropriate consent.

c) Before supplying non-identifiable tissue for use in research, the tissue bank must ensure that:
   i) An IRB has approved the proposed research that the tissue would be used for or the tissue bank is satisfied that there is scientific merit for the proposed research; and
   ii) There is documentary evidence provided by the receiving party that the receiving party will ensure that the intended use of the tissue is in accordance with any restrictions/conditions of the donors' appropriate consent.

9.3.1.4 Export of Human Tissue

a) Before exporting any individually-identifiable tissue from Singapore, the tissue bank must ensure that:
   i) Appropriate consent has been obtained from the donor for the export or removal, as the case may be; and
   ii) There is documentary evidence provided by the receiving party that the receiving party will ensure that the intended use of the tissue is in accordance with any restrictions/conditions of the donors' appropriate consent.

b) De-identified tissue may be exported even if consent had not been obtained for its export from the tissue donor. However, if the donor had stipulated that he/she did not wish for his/her tissue to be exported, his/her wishes should be respected.

9.3.1.5 Import of Human Tissue

There must be documentary evidence (e.g., declaration in Material Transfer Agreement or Tissue Requisition forms etc.) that consent has been obtained in accordance with the legal or ethical requirements of the place where the tissue is imported from.

9.3.2 Key HTF Requirements for Consent

For consent involving deceased persons, please refer to Chapter 5.

For consent involving minors and persons lacking mental capacity, please refer to Chapter 6.

9.3.2.1 Requirements for Appropriate Consent

The requirements for appropriate consent is fulfilled when consent is obtained in:

a) In writing;
b) From the tissue donor personally or their legal representatives;
c) After the information referred to in HBRA section 12(2) has been provided and explained to the tissue donor or the persons authorised to give consent on the donor's behalf; and
d) In the presence of a prescribed witness

9.3.2.2 Tracking of Consent and Integrity of Records

A system must be established to ensure:

a) That every donor's consent in relation to each tissue under the supervision and control of the tissue bank is accurately tracked; and
b) The integrity of records of the consent and other information relating to the donor.

9.3.2.3. Exemptions for Appropriate Consent

The requirement for appropriate consent to be obtained from a tissue donor for the storage, supply and use of tissue in research may be exempted if **ALL** the conditions below are met—

a) The tissue was removed from a human body any time before 1 November 2019;

b) There is documentary evidence indicating that relevant consent has been obtained in writing, after the minimal set of "core" information as follows has been provided and explained:

    i) 12(2)(a) specific research purpose for which the tissue is intended to be used, if this information is available, otherwise, the purpose may be stated as for general research;
    ii) 12(2)(f) the donor's right to withdraw his or her consent and the limitations of such withdrawal; and
    iii) 12(2)(i) the extent to which donor records will be kept confidential.

c) The relevant consent was not withdrawn any time before 1 November 2019.

9.3.2.4 Exemptions for Requiring a Prescribed Witness

The requirement for a witness to be present during appropriate consent from a tissue donor may be exempted in the following scenarios:

Scenario 1

The tissue:

a) Is removed primarily for a therapeutic or diagnostic purpose; and
b) Is not to be used for restricted human biomedical research.

Scenario 2

a) Tissue removal involves no more than minimal risk to tissue donor;
b) Tissue donor is able to read and sign the appropriate consent form; and
c) Appropriate consent is not for the purpose of restricted human biomedical research.

Scenario 3

The consent for the removal, storage, supply or use of tissue was given by a tissue donor before 01 November 2019.

9.3.3 Key HTF Requirements for Tissue Banks that Support Transplantational Research

9.3.3.1 Documentation

Every transplantational tissue bank must maintain a record containing a detailed description of the condition of each tissue under its supervision and control, including any observed tissue abnormalities or imperfections.

9.3.3.2 Tracking of Information Relevant to the Safety and Quality of Human Tissue

Every transplantational tissue bank must establish a system to ensure that the information relevant to the safety and quality of each tissue under its supervision and control is accurately tracked.

9.3.3.3 Additional Requirements Before Tissue is Released, Supplied or Exported

Before tissue is released, supplied or exported by a transplantational tissue bank:

a) The principal person in charge must authorize the release, supply or export of the tissue in writing; and
b) The transplantational tissue bank must ensure that the following information is provided to the researcher receiving the tissue:
    i) Source of tissue;
    ii) Donor screening process and tests conducted to ensure product safety and compatibility; and
    iii) Any regulatory obligation of the tissue bank as a result of the removal, supply or export of the tissue

9.3.3.4 Notification by Recipient of Human Tissue

Every transplantational tissue bank must ensure that the recipient of human tissue stored or supplied by the tissue bank is informed in writing to notify the tissue bank immediately of any suspected transmission of a communicable disease through transplanted tissue or a serious adverse event (SAE). The tissue bank must in turn make a notification of SAE or untoward occurrence associated with the removal of human tissue primarily for research to MOH.

9.3.3.5 Management of tissue contamination

Every transplantational tissue bank must establish a system to prevent or control the spread of any communicable disease which is or may be due to the contamination or infection of any tissue under its supervision and control. This system must at the minimum take into consideration the following:

a) Traceability of tissue;
b) Traceability of equipment and material used to process the tissue;
c) Processing and preservation of tissue;
d) Recall procedure for tissue.

9.3.3.6 Quality and safety management systems

a) Every transplantational tissue bank must establish a system to ensure the quality and safety of any tissue intended for use in human transplantation under its supervision and control. This system must at the minimum take into consideration the following:
    i) Qualification and training of personnel handling tissue;
    ii) The method of processing and preservation to retain the biological function compatible with its intended use;
    iii) Appropriate labelling and storage conditions;

iv) Management of quality control and inventory;
v) Suitability and testing of tissue donors.

b) An appropriate and effective system must be established to ensure the recall of tissue which had been unintentionally or otherwise erroneously supplied for use in research involving human tissue transplantation.

9.4 Serious Adverse Event / Untoward Occurrence Reporting

9.4.1 Definitions of SAE and UO

Serious Adverse Event (SAE) - Any occurrence associated with the procurement, testing, processing, storage or distribution of **human tissue (including gametes or embryos) intended for human application (i.e. human transplantation)** which:

a) Results in or contributes to death;
b) Is life-threatening;
c) Requires in-patient hospitalisation or prolongation of existing hospitalisation;
d) Results in or contributes to persistent or significant disability or incapacity;
e) Results in the transmission of a communicable disease; or
f) Results in any misidentification or mix-up of any type of tissue, gametes or embryo.

Untoward Occurrence (UO) - Any occurrence associated with the **removal of human tissue primarily for research** that:

a) Results in or contributes to death;
b) Is life-threatening;
c) Requires in-patient hospitalisation or prolongation of existing hospitalisation;
d) Results in or contributes to persistent or significant disability or incapacity;
e) Results in the transmission of a communicable disease;
f) Results in any misidentification or mix-up of any type of tissue, gametes or embryo; or
g) Results in or contributes to a congenital anomaly or birth defect.

9.4.2 SAE / UO Assessment

The custodian / TCA must review the event and assess the causality of the event and the type and severity of harm / potential harm:

a) Causality – The custodian / TCA should evaluate the causal relationship between SAE / UO and tissue banking activity. The expression 'reasonable causal relationship' is meant to convey in general that there are facts (evidence) or arguments to suggest a causal relationship. The following conditions might help to assess causality:
    (i) The event has a reasonable temporal relationship to the tissue banking activities,
    (ii) The event could not have been produced by the underlying disease states,
    (iii) The event could not have been due to other non-tissue bank interventions,
    (iv) The event follows a known pattern of response to the tissue banking activities, or
    (v) The event disappears with cessation of tissue banking activities.

b) Type and severity of harm / potential harm – The custodian / TCA must evaluate the type and severity of harm caused to the safety (e.g., physical hurt is caused) & welfare (e.g., feeling threatened or humiliated, breach of confidentiality or the invasion of privacy, incurring cost without consent of the tissue donor / recipient, affecting one's autonomy) of tissue donors & recipients.

For information on the SAE / UO reporting process, NHG Health custodians may refer to **Section 9.7.4 SAE / UO Reporting**.

For custodians / TCAs from non-NHG institutions, please check with your research office / relevant institutional authority on the non-compliance / SOC reporting process.

9.5 Suspected Offence or Contravention (SOC) Reporting

A non-compliance refers to the failure to abide by the approved protocol, the relevant institutional requirements or applicable regulations governing the protection of tissue donors. An SOC refers to any **non-compliance to the legal provisions set out in the HBRA and its Regulations**. Hence, not all non-compliances are SOCs and non-compliances reported by the custodian / TCA would need to be assessed by the RI / TB to determine if it is an SOC reportable to MOH.

For more information on the non-compliances reporting process, NHG Health custodians may refer to **Section 9.7.3 Non-compliances Reporting**.

For custodians / TCAs from non-NHG institutions, please check with your research office / relevant institutional authority on the non-compliance / SOC reporting process.

9.5.1 Assessment of SOCs

An SOC would be deemed reportable to MOH if it has resulted in harm or had the potential to cause harm to the safety and welfare of tissue donors. The following scenarios are examples of "harm" to the safety and welfare of tissue donors:

a) Physical hurt is caused
b) Mental and emotional distress such as feeling threatened or humiliated
c) Breach of confidentiality or the invasion of privacy
d) Incurring cost without consent
e) Affecting one's autonomy

9.6 Cessation of Tissue Bank Operations

The custodian must notify the TCC (For NHG Health custodians) or equivalent (For non-NHG custodians) on the intention to cease operating. For NHG Health custodians, this is performed by submitting a completed tissue bank status report form to NHGTCCSecretariat@nhg.com.sg.* The TPIC or designee will notify the Director of MOH in the applicable form set out at the relevant website as soon as possible and in any event not less than 30 days before the cessation of operation.

The notification will include:

a) Disposal plan for the human tissue samples and information related to such tissue;
b) Date and reason for cessation
c) Where the plan involves the transfer of the human tissue or information related to the tissue to another tissue bank, it should also include –
   (i) Name, address and contact details of the receiving tissue bank; and
   (ii) Documentary evidence provided by the receiving bank that the receiving bank will ensure that the intended use of the tissue is in accordance with any restrictions specified by the donors during consent-taking;
d) Any other information as required by the Director of MOH

NOTE: For non-NHG custodians, please check with your relevant institutional authority / research office on the notification process for cessation of tissue banks.

9.6.1 Preparation for Tissue Bank Closure

In preparation for the closure of a tissue bank, the custodian and/or designee must ensure the following (but not limited to) are performed or resolved:

a) All data queries received to date have been resolved to the fullest extent possible.
b) All reportable events (e.g. Serious Adverse Events (SAEs), untoward occurrences (UOs), non-compliances) have been submitted to the TCC or equivalent and sponsor (if applicable).
c) All essential documents (e.g. original signed informed consent forms, data collection forms) are filed in the tissue bank file and databases are complete and available for transfer or archiving.
d) Any unused tissue bank supplies and/or equipment are destroyed or returned to sponsor (if applicable).
e) Tissue samples are reconciled and tissue specimen logs are up to date.
f) Where applicable, ensure a Material Transfer Agreement of equivalent is established before transferring the entire tissue collection to another tissue bank or a new custodian.

g) Where applicable, ensure that the transfer or tissue samples and tissue bank documents to another tissue bank or a new custodian is carried out in accordance to the HBRA requirements.
h) All used and unused tissue samples are disposed in accordance to institutional guidelines / SOPs if they are to be destroyed.
i) Upon closure of the tissue bank, if the custodian needs to keep the data for future research use, the custodian should follow institutional and regulatory requirements for retaining the tissue bank data.

9.7 Submissions to the NHG Health Tissue Compliance Committee (TCC)

IMPORTANT: Section 9.7 is only applicable to custodians from NHG Health Institutions. For custodians from non-NHG institutions, please check with your research office / relevant institutional authority on the required submission and their respective processes and timelines.

In addition to the initial registration of tissue banks and tissue collections (Refer to **Section 9.3**) tissue custodians / tissue collection applicants from NHG Health institutions would also be required to perform the following submissions to the TCC.

a) Tissue Bank / Tissue Collection Amendments
b) Continuing Review
c) Non-Compliances Reporting
d) SAE / UO Reporting

The relevant forms for the above submissions can be downloaded from the NHG Health Research Website. These documents are strictly for internal circulation among NHG Health Staff and Authorized personnel only.

9.7.1 Tissue Bank / Tissue Collection Amendments

No deviation from, or changes of the tissue banking activities should be implemented without documented approval from the TCC, except where necessary to eliminate apparent immediate hazard(s) to the donors, or when the change(s) involves only logistical or administrative aspects of the tissue bank (e.g., change of telephone number).

Any deviation from, or a change of, the protocol to eliminate an immediate hazard should be promptly reported to the TCC as soon as possible but not later than 7 calendar days upon first knowledge by the custodian / tissue collection applicant. For more information, please refer to **Section 9.7.3 Non-Compliances Reporting**.

For tissue bank / tissue collection amendments, the following must be submitted

i. Tissue Bank Amendment / Tissue Collection Amendment Form
ii. Any amended documents
iii. Any other relevant documentation when, in the judgment of the TCC or the IRB, the additional information would add meaningfully to the protection of the rights, safety and wellbeing of the tissue donors
iv. Any other documentation that the TCC may specifically request

9.7.2 Continuing Review

The TCC will conduct continuing review of ongoing tissue banks and tissue collection protocols once per year. Continuing TCC review is required as long as tissues are stored in the tissue bank.

Approvals for Tissue Banks / Tissue Collections expire on 28 February each year. Custodians are strongly advised to submit a duly completed Tissue Bank Status Report Form and/or Tissue Collection Status Report Form to the TCC at NHGTCCSecretariat@nhg.com.sg **between** 01 January to 31 January to allow sufficient time for the TCC to process the application prior to Tissue Banks/ Tissue Collections approval expiry. The information provided in the status report form should cover for the period between 01 January to 31 December of the preceding year.

Tissue Banks or Tissue Collections that were reviewed by the full Quorum and determined to require a higher frequency of continuing reviews at shorter intervals due to the high degree of risks involved must additionally submit their status report forms at the intervals set on by the Quorum.

The custodian / TCA is responsible for submitting the status reports for continuing review before the expiration date and in ample time for the TCC review. If the custodian / TCA fails to submit the status reports for an active Tissue Bank / Tissue Collection, or if the TCC has not reviewed and approved the submitted status reports by the expiration date, the Tissue Bank / Tissue Collection will be considered lapsed and all tissue banking activities will be required to cease immediately.

If tissue banking activities were performed during the lapse of TCC approval, the custodian / TCA will be required to submit a non-compliance report to the TCC by using a Tissue Non-Compliance/ Protocol Deviation Report Form to document activities that were conducted during the lapse.

9.7.2.1 Supporting Documents for Continuing Review

The custodians / TCAs applying for renewal of approval of a tissue bank / tissue collection must provide the following information to the TCC (where applicable):

Tissue Bank Status Report

a) SAEs/ UOs since last review;
b) Non-compliances/ deviation reports since last review;
c) Tissue Bank protocol amendments since last review;
d) Potential conflicts of interest since the last review;

e) Any other relevant information, especially information about compliance adherence associated with the Tissue Bank.

Tissue Collection Status Report

a) Donor recruitment;
b) Number and reasons for withdrawal of donors;
c) SAEs/ UOs since last review;
d) Non-compliances/ deviation reports since last review;
e) Tissue Collection protocol amendments since last review;
f) Complaints about the tissue collection and related activities;
g) Any other relevant information, especially information about the risks associated with the tissue collection.

9.7.2.2 Tissue Bank / Tissue Collection Status Reporting

The custodian or TCA must also indicate the status of the tissue bank and tissue collection, where applicable, details of each as follows:

Status of Tissue Bank

a) Ongoing. No new tissue to be added (maintenance of existing tissues only).
b) Ongoing. New tissues may be added from DSRB-approved studies/ DSRB-acknowledged tissue banks.
c) Ongoing. New tissues may be added from TCC-approved Tissue Collections.
d) Suspended
e) Terminated
f) Closed

Status of Tissue Collection

a) Ongoing (Recruitment of new donors ongoing)
b) Ongoing (Recruitment closed, enrolled donors on follow up either for ongoing tissue collection or data collection)
c) Not yet initiated (Pre-screening and recruitment process not started yet)
d) Suspended
e) Terminated
f) Completed
   (i) The Tissue Collection is permanently closed to the recruitment of new donors
   (ii) All enrolled donors have completed their tissue donation
   (iii) Collection data for all enrolled donors has been completed

9.7.3 Non-Compliances Reporting

9.7.3.1 Definition of Non-Compliance

Non-compliance is a failure to abide by the approved protocol, the policies and procedures of the TCC, the relevant institutional requirements, or applicable regulations governing the protection of tissue donors. Some examples of non-compliance include failure to (but are not limited to):

a) Obtain approval for operating a Tissue Bank/initiating tissue collection
b) Obtain renewal of approval for a Tissue Bank/Tissue Collection Protocol,
c) Obtain appropriate informed consent when required,
d) File a SAE/UO report,
e) Submit amendment(s) for review and approval,
f) Adhere to the approved protocol,
g) Adhere to the regulations, policies, and procedures related to tissue banking activities.

9.7.3.2 Non-Compliance Assessment

The custodian / TCA must review the non-compliance and assess whether the event arises in relation to tissue banking activities conducted under the supervision and control of the tissue bank or tissue collection. The custodian / TCA must also assess the type and severity of harm / potential harm caused to the safety (e.g. physical hurt is caused) & welfare (e.g. feeling threatened or humiliated, breach of confidentiality or the invasion of privacy, incurring cost without consent of the tissue donor/ recipient, affecting one's autonomy) of tissue donors & recipients.

9.7.3.3 Non-Compliance Reporting Process

The custodian / TCA must report any non-compliances to the TCC by submitting a completed Tissue Non-Compliance/ Protocol Deviation Report Form to NHGTCCSecretariat@nhg.com.sg.

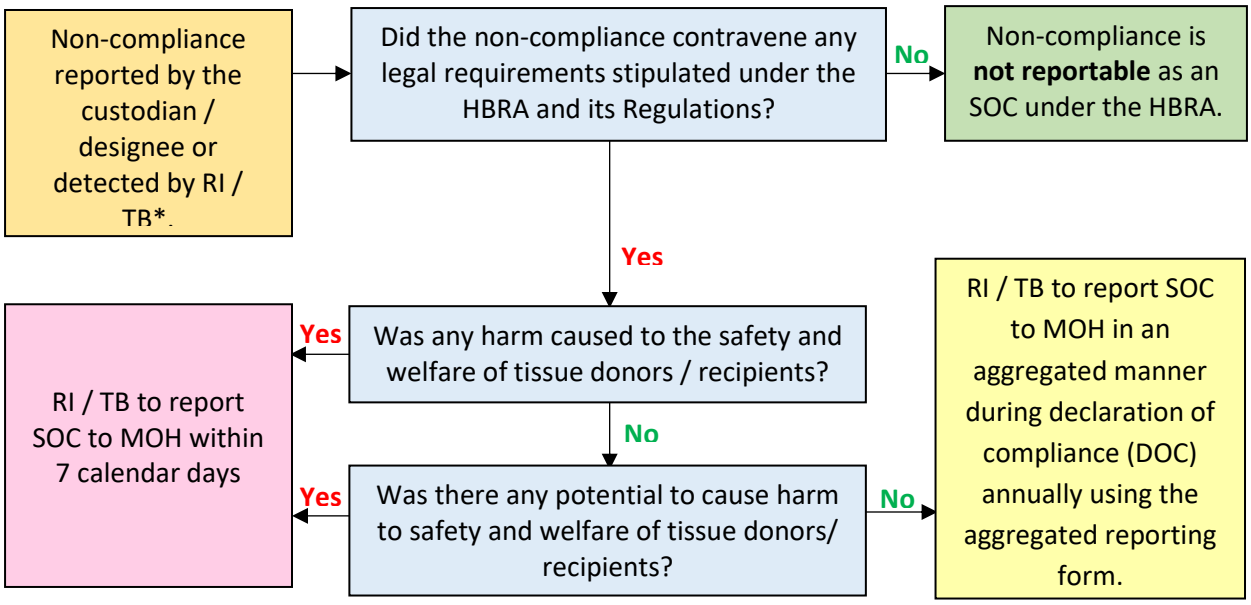
9.7.3.4 Non-Compliance Reporting Timelines.

a) The custodian / TCA or designee must report any non-compliance to the TCC as soon as possible but not later than 7 calendar days after first knowledge by the custodian / TCA.

b) If the non-compliance was assessed to contravene any of the legal requirements stipulated under the HBRA and its Regulations and had caused harm or had the potential to cause harm

to the safety and welfare of tissue donors, the TPIC or designee would need to submit the information to the Director of MOH in the applicable form set out at the relevant website as soon as possible and in any event not later than 7 calendar days after the tissue bank or TPIC or designee first becomes aware of the information. Refer to **Figure 12** for the workflow on assessing and reporting Suspected Offence and Contravention (SOC).

Figure 12: Workflow for assessing and reporting SOC



Note: The RI / TB refers to the relevant institutional authority that governs all institutional tissue banks. For NHG Health institutions, this refers to the NHG Health Tissue Compliance Committee (TCC).

Please refer to **Section 9.5 Suspected Offence or Contravention (SOC) Reporting** for more information.

9.7.4 SAE / UO Reporting Process

The NHG Health custodian / TCA or designee is responsible for the timely reporting of any SAE / UO to the TCC by submitting a completed SAE / UO Report Form to NHGTCCSecretariat@nhg.com.sg. The Tissue Principal Person In Charge (TPIC) or designee will review and submit the information to the Director of MOH, if necessary.

9.7.4.1 SAE / UO Reporting Timelines

a) Results in death or is life-threatening

(i) NHG Health custodians / TCAs must submit all recorded information on the SAE / UO to the TCC **immediately after first knowledge** by the custodian, and any additional relevant information should be reported to the TCC **as soon as possible** after the record is made.

(ii) The TPIC or designee will review and submit the information to the Director of MOH in the applicable form set out at the relevant website as soon as possible and in any event not later than **7 calendar days** after the tissue bank or the TPIC or designee first becomes aware of the event, whichever is the earlier; and any additional relevant information about the SAE is recorded and submitted to the Director of MOH **within 8 days** after the record is made.

b) Does not result in death and is not life-threatening

(i) NHG Health custodians / TCAs must submit all recorded information on the SAE / UO to the TCC **immediately** after first knowledge by the custodian, and any additional relevant information should be reported to the TCC **as soon as possible** after the record is made.

(ii) The TPIC or designee will review and submit the information to the Director of MOH in the applicable form set out at the relevant website as soon as possible and in any event not later than **15 calendar days** after the tissue bank or the TPIC or designee first becomes aware of the event, whichever is the earlier.

The SAE / UO reporting requirements are summarized in **Table 15**.

Table 15: Summary of SAE / UO reporting requirements

	SAE / UO resulting in death or is life-threatening	**SAE / UO which does not result in death and is not life-threatening**
Timeline for Initial Report to TCC	Immediately after first knowledge by the custodian	
Timeline for Follow-Up Report to TCC	As soon as possible after the initial report	
Timeline for Initial Report to MOH	As soon as possible but not later than 7 calendar days after the tissue bank or the TPIC or designee first becomes aware of the event	As soon as possible but not later than 15 calendar days after the tissue bank or the TPIC or designee first becomes aware of the event
Timeline for Follow-Up Report to MOH	Within 8 days after the initial report	**-**

9.8 Tissue Bank Essential Documents

The custodian / TCA should maintain a tissue bank file containing essential documents. The purpose of maintaining essential documents is to keep an audit trail on the management of human tissue from its collection, processing, storage, supply and destruction (where applicable). Essential documents would also allow the monitors, auditors and inspectors to confirm the compliance of tissue banking activities with the applicable regulatory requirements and institutional policies and SOPs.

Essential documents may be grouped into the various categories. The essential documents in these categories include (but are not limited to) the following:

b) Tissue Compliance Committee (TCC) or equivalent (For Non-NHG institutions) documents
   i. Approval letters
   ii. Initial application forms and documents submitted and approved by the TCC or equivalent
   iii. Amended application forms, amendment cover note or amendment summary
   iv. TCC or equivalent approved amended documents
   v. Annual Tissue Bank Status Report Forms
   vi. Serious Adverse Event (SAE), Untoward Occurrence (UO) and Non Compliance reports

c) Tissue Bank Team
   i. Contact details of tissue bank staff
   ii. Tissue Bank Responsibility / Delegation log
   iii. Curriculum Vitae (CV) of all tissue bank team members
   iv. Copy of training certification for all tissue bank team members
   v. Training documentation (e.g., training record form(s), training slides)

d) Laboratory
   i. Specimen collection/ processing/ request/ retrieval/ destruction records
   ii. Specimen procurement records
   iii. Specimen Inventory logs
   iv. Shipping records (e.g., courier shipment receipts, shipment tracking log)
   v. Equipment maintenance records (e.g. calibration certificates)
   vi. Temperature logs

e) Other documents
   i. Donor Screening / Enrolment / Identification logs
   ii. Signed informed consent forms
   iii. Monitoring documents (e.g. monitoring reports)
   iv. Significant correspondences

v. Tissue bank collaboration agreement (e.g. Material Transfer Agreement)

NHG Health researchers may refer to the PCT 1501-01 Tissue Bank File Contents Template on the NHG Health Research Website (https://www.research.nhg.com.sg) for a full list of essential documents to be maintained in the tissue bank file. The essential document templates, logs and forms can also be downloaded from the NHG Health Research Website*.

NOTE: These document downloads can only be accessed when you have direct access to the NHG Health Intranet. These documents are strictly for internal circulation among NHG Staff and Authorized personnel only.