FAQs ON HUMAN BIOMEDICAL RESEARCH ACT

Contents

General 2

Scope of Human Biomedical Research 4

Sensitive Research 7

Regulation of Human Biomedical Research 8

(A) Institutional Review Boards 9

(B) Research Institution 11

(C) Researchers 13

Consent for Human Biomedical Research 16

Human Biomedical Research Compared with Clinical Trials Regulations 18

Scope of Human Tissue 19

Regulation of Tissue Banking Activities 20

Consent for Tissue Donation 23

General

Q1: What are the objectives of the Human Biomedical Research Act (HBRA)?

The Act sets out the regulatory frameworks for (i) human biomedical research, and (ii) human tissue for use in research.

The objectives of the Human Biomedical Research Framework are:

1. To regulate human biomedical research with the aim of protecting the safety and welfare of human research subjects.

2. To regulate the conduct of certain types of human biomedical research that are considered more 'sensitive', such as research involving human eggs or embryos, or human-animal combination embryos, regardless of the risk posed to human research subjects.

The objectives for the Human Tissue Framework are:

1. To protect the safety and welfare of tissue donors (such as mandating informed consent from donors, ensuring altruistic donations and that donors' health and welfare are not jeopardised).

2. To prohibit commercial trading of human tissue (regardless of whether or not it is to be used for research)

Q2: What are the main elements and aspects covered in the Act?

The Act will:

(a) define the scope of human biomedical research and human tissue that will be regulated under the Act;

(b) identify the different key players in the biomedical research environment, including the entity known as the "research institution", and define their relationships with one another;

(c) strengthen governance over human biomedical research by specifying the inter-related roles and responsibilities of the individual researcher, the institutional review board, and the research institution;

(d) stipulate the requirements that must be fulfilled before any person may conduct human biomedical research;

(e) stipulate the requirements that must be fulfilled before any person may remove, store, supply or use human tissue for research;

(f) prohibit the commercial trading of human tissue and coercion to participate in research; and

(g) formalise the system of internal reviews and 'checks-&-balances' for research institutions and tissue bank.

Q3: When was the Act implemented?

The Human Biomedical Research Act was passed in Parliament in 2015 and operationalised in phases. The provisions relating to the prohibition against commercial trading of human tissue came into force on 1 January 2017, followed by the provisions relating to the Human Biomedical Research Framework on 1 November 2017. A one year 'sunrise period' was provided for affected parties to make the transition. Existing human biomedical research studies involving the use of health information and or human biological material were permitted to continue without the need to re-consent if certain conditions are met. The details can be found in the Guidance on the Requirement of Appropriate Consent for the Conduct of Human Biomedical Research and Handling of Human Tissue here.

The remaining provisions in the Act relating to the regulation of tissue banks and tissue banking activities were fully activated on 1 November 2019. A complete listing of the Act and its subsidiary legislation can be found here.

Scope of Human Biomedical Research

Q4: What is the scope of human biomedical research covered in the Act?

The scope of research that will be regulated under the Act includes two main areas:

1. Research that is intended to study –

    (a) the prevention, prognostication, diagnosis or alleviation of any disease, disorder or injury affecting the human body; OR

    (b) the restoration, maintenance or promotion of the aesthetic appearance of human individuals through clinical procedures or techniques; OR

    (c) the performance or endurance of human individuals,

AND where the research involves –

    (i) subjecting an individual to any intervention (including any wilful act or omission) that has a physical, mental or physiological effect (whether temporary or permanent) on the body of the individual; OR

    (ii) the use of any individually-identifiable biological material obtained from the human body; OR

    (iii) the use of any individually-identifiable health information.

2. Research that involves –

    (a) human embryos or human gametes; OR

    (b) cytoplasmic hybrid embryos; OR

    (c) the introduction of any human-animal combination embryo into an animal or a human; OR

    (d) the introduction of human stem cells (including induced pluripotent stem cells) or human neural cells into an animal at any stage of development (including a pre-natal animal foetus or animal embryo); OR

    (e) any entity created as a result of any process referred to in paragraph (c) or (d).

In the case of area (1) above, research that is not intended for any of the medical- or clinical-related purposes described in (a), (b) or (c) (e.g. research to study educational pedagogy, consumer preference surveys or cognitive, aptitude or I.Q. tests) will not be regulated as human biomedical research. Similarly, biomedical research that does not involve any of the methodologies described in (i), (ii) or (iii) (e.g. research using only aggregated or anonymised health data, elasticity testing of de-identified tissue, etc.) will also not be regulated as human biomedical research under this Act.

You may wish to use the Human Biomedical Research Decision Tool found here for a preliminary assessment on whether your study fulfils the definition above.

Q5: Are medical device trials regulated under the Act?

Medical device clinical trials are required to comply with the requirements of the Human Biomedical Research Act if they fulfil the definition of human biomedical research in section 3 of the Act (refer to definition in Q4).

HSA also regulates the import, manufacture, export and supply of medical devices in Singapore, under the Health Products Act. Medical devices must be registered with HSA before they can be sold or supplied in Singapore, unless they are Class A devices which are exempted from product registration. Registered devices should only be used in accordance with the intended purpose and indications for use as registered with HSA.

In addition, the manufacture, import and supply of medical devices used as clinical research materials (CRM) in Singapore must comply with the regulatory controls for CRM under the Health Products Act or Medicines Act. Researchers may refer to the guidance here for more information pertaining to CRM notification.

Q6: Are there any prohibited or restricted categories of human biomedical research?

The Act identifies two sub-categories of human biomedical research, namely "restricted research" and "prohibited research".

Restricted Research

These are types of human biomedical research that are considered to be more 'sensitive' in nature, and need to be controlled more tightly. At present, these include research that involve human procreation, or may possibly create human sentience in animals. The current list of "restricted research" includes the following:

1. Human biomedical research involving human eggs or human embryos.
2. Human biomedical research involving –
   (a) cytoplasmic hybrid embryos;
   (b) embryos created by using —
      (i) human gametes and animal gametes, or
      (ii) one human pronucleus and one animal pronucleus;
   (c) the introduction of human stem cells (including induced pluripotent stem cells) into a pre-natal animal foetus or animal embryo;
   (d) the introduction of human pluripotent stem cells (including induced pluripotent stem cells) into a living post-natal animal but excludes the introduction of such human pluripotent stem cells into immunodeficient mice solely for the analysis of teratoma induction;

(e) the introduction of human stem cells (including induced pluripotent stem cells) or human neural cells into the brain of a living post-natal animal; or

(f) any entity created as a result of any process referred to in paragraphs (c) to (e).

Restricted research will be subject to additional regulations on top of the requirements for human biomedical research in general. For example, a researcher who intends to conduct any restricted research will need to get approval not only from the institutional review board, but also from HSA. For such matters, HSA will have an expert committee to review and provide guidance on whether the proposed restricted research should be allowed.

Where the research involves the use of animals, additional approval will also need to be sought from the Institutional Animal Care and Use Committee (IACUC).

Prohibited Research

These types of human biomedical research are deemed to be unacceptable and will not be allowed in Singapore. The current list of "prohibited research" includes the following examples:

1. Human biomedical research involving the development of cytoplasmic hybrid embryos beyond 14 days or the appearance of the primitive streak, whichever is the earlier.

2. Human biomedical research involving the implantation —

(a) of the following types of human-animal combination embryo into the uterus of an animal:

(i) cytoplasmic hybrid embryos, or

(ii) human-animal combination embryos created in-vitro by using:

(A) human gametes and animal gametes; or

(B) one human pronucleus and one animal pronucleus the development of human-animal combination embryos.

(b) of a human-animal combination embryo into the uterus of a human.

3. Human biomedical research involving the introduction of human stem cells (including induced pluripotent stem cells) or human neural cells into the brain of living great apes whether pre-natal or post-natal.

4. Human biomedical research involving the breeding of animals which have had any kind of human pluripotent stem cells (including induced pluripotent stem cells) introduced into them.

Note: There are four types of great apes: gorillas, bonobos, orangutans and chimpanzees.

Sensitive Research

Q7: What is the basis for prohibiting certain types of human biomedical research?

Research that presents a high risk of developing entities with human sentience or consciousness will not be allowed in Singapore under the Act.

The current list is adopted from the recommendations made by the Bioethics Advisory Committee, in its report on Human Animal Combination in Stem Cell Research 2010.

Q8: What is the basis for regulating human-animal combination research?

In relation to human-animal combination research, it is recognised that the greater the possibility of "humanisation" of the animal, the greater the need for restrictions. Hence, the Bioethics Advisory Committee has advised that a national committee be established to review research for all human-animal combination research in Singapore. In particular, attention should be paid to avoid the creation of entities with human sentience or consciousness.

Regulation of Human Biomedical Research

Q9: Who are the key entities in this regulatory framework for human biomedical research? How do they relate to one another in this framework?

The three key entities in the human biomedical research framework are (i) the individual "researcher", (ii) the "research institution", and (iii) the "institutional review board". Each of them has its respective roles and responsibilities within the framework, and they function together in an interlocking system of 'self-accountability'.

The research institution:

(a) exercises supervision and control over its researchers who conduct human biomedical research, including supervising and proactively monitoring their research to ensure that they comply with the regulatory requirements and controls; and

(b) appoints the institutional review board to review the research proposals of its researchers, and provides the necessary support to ensure the proper functioning of the institutional review board.

The institutional review board:

(a) reviews the research proposals of researchers who come under its appointing research institution, assessing (among others) the ethics of the study, the qualifications of the researcher(s), and the adequacy of the monitoring system and safety measures put in place to protect the research subjects; and

(b) considering the safety and welfare of the research subjects, makes an independent assessment as to whether to approve (or reject) the proposed research.

The researcher who conducts human biomedical research:

(a) must conduct his research under the supervision and control of a research institution;

(b) must get his research proposal reviewed and approved by an institutional review board appointed by his research institution;

(c) must ensure that appropriate consent is obtained from each research subject he enrols in his research; and

(d) in conducting his research, must not deviate from the approved research proposal unless the deviation has also been reviewed and approved by the institutional review board.

(A) Institutional Review Boards

Q10: What is an institutional review board? What is the role of the institutional review board in this regulatory framework?

The Act defines an "institutional review board" as a board or committee appointed by a research institution to conduct ethics review of proposed human biomedical research. Institutional review boards (or sometimes known as ethics review committees) are central to the framework of ethical governance in human biomedical research. The primary responsibility of institutional review boards is to protect the safety, dignity and welfare of human research subjects.

Q11: What is the relationship between an institutional review board and a research institution?

An institutional review board is appointed by a research institution. By the same token, a research institution is required to appoint an institutional review board to review the research proposals of researchers from its institution. Thus, the existence of these two entities is closely tied together.

It should be noted that under this framework, an institutional review board only conducts ethics reviews on research proposals of researchers who come under the supervision and control of the appointing research institution, and any approval by the institutional review board is only valid in that context.

Q12: What are the requirements on the composition of an institutional review board appointed under the Act?

The institutional review board members should be individually appointed by the research institution. The institutional review board should comprise a minimum of five individuals in order to reach a quorum, including one chairman (who must be a locally registered medical practitioner), at least one external scientific person, and at least one external lay person.

'Scientific person' refers to a person with a professional scientific or clinical qualification, knowledge or experience so as to enable the person to assist the institutional review board in understanding particular aspects of the research proposal under review by the board.

'Lay person' refers to a person who does not fall within any of the following:

(a) An individual who is or was a healthcare professional;
(b) An individual who possesses or previously possessed a qualification or registration, in a country or territory outside Singapore, which is equivalent to or corresponds with any of the qualifications in paragraphs (a) to (f) of the definition of "healthcare professional" in Regulation 2 of the Human Biomedical Research Regulations 2017;
(c) An individual who is currently or was previously involved in the conduct of any research as an investigator.

A person is treated as external in relation to a research institution if the person is not a researcher of, not employed by and not in a commercial relationship with the research institution. A person would be considered to be in a “commercial relationship” with the research institution if he/she has any on-going, for-profit transactions with the research institution, e.g. tenant-landlord, sponsors, shareholders.

Q13: Can a researcher whose project was rejected by one institutional review board seek a second review by another institutional review board?

Where a research proposal has been reviewed but has not been approved by an institutional review board, the researcher may appeal to his research institution for a further review of the research proposal. No appeal is allowed unless the first board has confirmed in writing that it has disallowed the conduct or continuation of the research.

The research institution will have the discretion to allow the proposal to be reviewed again, whether by the same institutional review board or another institutional review board appointed by that research institution. In other words, whether the second review is conducted by another institutional review board is at the discretion of his/her research institution.

Q14: Can the institutional review board review studies that are not human biomedical research?

There is no requirement under the Act for studies that are not human biomedical research to be reviewed and approved by the institutional review board. Notwithstanding, the institutional review board may conduct the review of such studies as per the agreement or arrangement between the research institution and its institutional review board. For such reviews, the composition requirements of the institutional review board under the Act will not apply.

(B) Research Institution

Q15: What is a research institution? What is the role of the research institution in this regulatory framework?

The Act defines a "research institution" as a body of persons, whether corporate or unincorporated, or other organisation, or ministry or department of the Government, who or which:

(a) engages directly or indirectly (either through contractual or other arrangements), one or more researchers to conduct human biomedical research in Singapore; and

(b) exercises supervision and control over human biomedical research conducted in Singapore by the researchers the institution has engaged.

The research institution is at the centre of the system of 'self-accountability' in this regulatory framework. Besides exercising supervision and control over the human biomedical research conducted by its researchers, the research institution also has to appoint the institutional review board to conduct an independent ethics review of the research proposals, and is responsible for providing all the necessary support to ensure that the institutional review board is set up and functions properly.

Q16: If an organisation or entity has its own institutional review board, does it mean it is a research institution?

No. Appointing an institutional review board and supporting its functioning does not automatically make that organisation a research institution. A research institution is essentially defined by virtue of the duties and responsibilities that it performs, and the role that it plays vis-à-vis researchers.

An organisation that intends to take on the role of a research institution is required to notify HSA before it commences operation as a research institution. This should be done through the TIARAS (Tissue and Research Application System) no later than 30 days before the commencement of the first human biomedical research. You may refer to the TIARAS Screenshots for Notifications (Research Institution) for a step-by-step guide on how to notify as a research institution.

Subsequently, the organisation is also required to submit a declaration of compliance to HSA on a date between 1st March and 18th April (both dates inclusive) of every year, as long as it continues operating as a research institution.

Q17: Must the research institution be located in Singapore?

Yes. An organisation that intends to take on the role of a research institution must be physically located in Singapore.

Q18: Can the research institution be located overseas and have a branch office in Singapore?

An organisation that intends to take on the role of a research institution must have a physical presence in Singapore. This is to ensure that all human biomedical research activities carried out in Singapore would be under the supervision and control of a research institution in Singapore, and subject to our laws.

If an overseas institution has a branch office in Singapore, and the branch office intends to conduct human biomedical research activities, it must either collaborate with a local research institution or establish itself as a research institution by notifying HSA of its intentions to commence operation as a research institution. The branch office must ensure that it has the capability and resources to fulfil the requirements of the Act for overseeing all human biomedical research conducted under its auspices. This oversight extends across all its research sites, and it starts from the point a proposed research protocol is submitted for review to the point that the research is completed or otherwise stopped.

Q19: Can a researcher be a research institution?

No. A researcher, by himself, cannot be a research institution. By definition, a research institution comprises at least two or more persons. The rationale is that a single person is unlikely to fulfil all the duties and responsibilities expected of a research institution.

Furthermore, it is necessary to have another party (other than the researcher himself) as the research institution, in order for there to be independent supervision and control over the researcher's work.

Q20: What should the research institution do if it no longer has any human biomedical research?

If the research institution has no intention to conduct further human biomedical research, it could notify HSA of its intention to cease operation as a research institution. The notification must be made through TIARAS with the information required in Regulation 10A of the Human Biomedical Research Regulations 2017 not less than 30 days before the intended date of cessation.

If the research institution has intention to conduct human biomedical research in the future, it could choose to remain as a research institution. However, the research institution will need to continue to comply with the duties and responsibilities of a research institution under the Act, including the submission of declaration of compliance annually with its accompanying fee. It may also be subject to regulatory audits by HSA.

(C) Researchers

Q21: What is the relationship between a researcher and a research institution?

A researcher can only conduct human biomedical research under the supervision and control of a research institution. In this regard, the researcher could be an employee of the research institution, or the researcher could be engaged by the research institution through some other arrangement, such as an agreement with the researcher to carry out an *ad hoc* research project under supervision and control of the research institution.

Researchers who do not have a formal affiliation with any research institutions would need to make the necessary contractual or other arrangement with a research institution e.g. a research collaboration agreement signed between the researcher's organisation and the research institution, so that the proposed research can be conducted under the supervision and control of that research institution.

Q22: What should I do if I wish to start a human biomedical research?

You should ensure that there is a research institution that is willing to supervise the conduct of your study. You will then need to submit your research application to the research institution's appointed institutional review board for review and to assess if your study is indeed a human biomedical research. Upon obtaining the institutional review board's approval, you may start to conduct your study or the recruitment of research subjects.

As a researcher, you should also be familiar with the duties of researchers as prescribed in section 22 of the Act in the conduct of your human biomedical research. You may refer to our website here for the Human Biomedical Research Act and other resources relating to the Human Biomedical Research Framework.

Q23: Will HSA be issuing licences for researchers to conduct research?

No, HSA will not license individual researchers. The proposed regulatory framework operates on a system of 'self-accountability', with 'checks and balances' in the system provided by the research institution and the institutional review board, who oversee the researchers conducting the human biomedical research.

Q24: What are the additional requirements for the conduct of restricted research?

For the conduct of restricted research, approval from HSA would need to be sought in addition to approval from the institutional review board. The restricted research application must be submitted to HSA via TIARAS. Where the research involves the use of animals, additional approval from the Institutional Animal Care and Use Committee (IACUC) would also be required.

Q25: As a researcher, am I allowed to delegate or outsource my duties to other person(s) who may not be a named researcher on the project?

The Act does not prevent the researcher from delegating or outsourcing his/her duties. However, the researcher is at all times responsible and made accountable, to ensure that the duties imposed on him/her are discharged in compliance with the Act's requirements.

Q26: I am conducting a human biomedical research involving researchers from multiple entities. What should I take note of?

When conducting a collaborative research involving researchers across multiple entities, it is important to draw up a research collaborative agreement (RCA) to detail the parties involved, the research institution(s) that will be supervising the study and the appointed IRB(s) to review and approve the human biomedical research. Should there be more than one research institution and there is an agreement for the human biomedical research to be reviewed by a common institutional review board, the common institutional review board must be appointed by the research institutions. Alternatively, the human biomedical research may be separately reviewed by the institutional review boards appointed by each research institution.

The research institutions should specify in the RCA the responsibilities of each research institution, especially the reporting of any serious adverse events or suspected offences or contraventions arising from the collaborative research.

Q27: How does the Act deal with serious adverse events, untoward occurrences and suspected offences or contraventions? Under what circumstances will HSA intervene or put a stop to a research?

Under the Act, research institutions and tissue banks are required to report serious adverse events (SAEs), untoward occurrences and suspected offences or contraventions (SOCs) to HSA. For the definition and respective reporting timelines of SAEs and SOCs, please refer to the infographics found on our website.

In the event HSA becomes aware of any safety issues or problems concerning any on-going human biomedical research, it will have the power to investigate and to intervene, if necessary. These include powers to:

a) order a researcher or a research institution to suspend, and if necessary, to terminate the research;

b) require the researcher or research institution to take precautionary or remedial measures;

c) order a research institution to remove or replace a member of an institutional review board member, or to assign the research to be reviewed by another institutional review board of that research institution; and

d) prohibit a research institution from conducting any further research activities.

The Chief Executive may also prohibit a researcher from conducting any further human biomedical research activities if the researcher:

a) has been convicted of an offence under the Act;

b) has been convicted of an offence involving fraud, dishonesty or moral turpitude;

c) is determined to be not of good reputation or character or is otherwise unfit to conduct such research; or

d) is unable to perform his duties as a researcher for medical reasons.

Q28: What are incidental findings? Do all incidental findings have to be returned to the research subjects?

Incidental finding, in relation to human biomedical research, means a finding about a research subject that has potential health or reproductive importance to the research subject and is discovered in the course of conducting research but is unrelated to the purposes, objectives or variables of the study.

The Act allows research institutions to formulate and implement their own policy on whether or not the research subject should be re-identified and informed in the case of an incidental finding. Research institutions must inform its appointed institutional review board and researchers of this policy. Researchers should also inform the research subject on the possibility of incidental finding arising from the research, and seek the consent of the research subject should they wish to return any incidental finding, in accordance with the requirement in section 12 of the Act. If no incidental findings would be returned, the negative fact should still be conveyed to the research subject when obtaining appropriate consent.

Consent for Human Biomedical Research

Q29: Can consent be obtained remotely from the research subjects?

Yes, researchers may explore obtaining consent from research subjects remotely e.g. through teleconferencing or a verbal phone call. When obtaining appropriate consent remotely, the researcher should ensure that the requirements of appropriate consent in Part 3 of the Act have been met. Where the witness requirement has not been exempted, the witness should be present in the teleconferencing call when the researcher explains the research study to the subject and obtains his/her consent over the call. The consent obtained should also be duly documented, either by requesting the subject and witness to sign the consent form digitally on the same day, or requesting the subject to mail a signed physical consent form to the researcher. Where the consent taker, subject and witness cannot sign on the consent form on the same day, the reason should be documented.

Q30: Do I need a witness to be present for consent taking in all interventional human biomedical research?

With the introduction of the Human Biomedical Research (Requirements for Appropriate Consent – Exemption) Regulations 2019 on 1 November 2019, there is no need for a witness to be present during consent taking **if** the interventional research involves no more than minimal risk to the research subject, the subject is able to read and sign the appropriate consent form and the research is not restricted research.

Note:

- *Minimal risk, as defined under the Act, means the probability and magnitude of harm and discomfort anticipated in the research or the removal of HT that are not greater, in and of themselves, than those ordinarily encountered –*

  (a) in the daily life of normal and healthy persons; or

  (b) during the performance of routine physical or psychological examinations or tests.

- *Some examples of interventional procedures that are of minimal risk include blood pressure measurement, finger-prick test and nasopharyngeal/buccal swab.*
- *Impartial witness is not a requirement under the Act.*

Q31: How do I justify whether my human biomedical research meets the criterion of "greater public good" to be granted a waiver of appropriate consent by the IRB?

Generally, research can be considered to contribute to the **greater public good** if it falls under one of the following categories:

a. Epidemiology research or population-wide studies at national level or regional level with potential direct benefit to the public at large;

b. Research with apparent or tangible benefits with measurable outcomes to the public at large and may include those less privileged community or a sub-community; or

c. Research that contributes or could contribute to impact at national, regional or international level with potential impact on change in policy and prevailing standards on innovation, management and practice in healthcare and other human biomedical related fields.

The researcher should provide his/her justification on the above in order for the institutional review board to make a proper assessment of the request for a waiver. Researchers who are affiliated with the healthcare clusters (i.e., NUHS, NHGHealth and SingHealth) may also wish to check with their research offices for guidance on interpreting the criterion of “greater public good”.

Q32: I have obtained institutional review board’s waiver of requirement for appropriate consent under the Fifth Schedule to use the individually-identifiable human biological material obtained in my existing human biomedical research. Can I use the leftover material for my future human biomedical research?

The waiver of appropriate consent is study specific. A fresh approval from the institutional review board would be required in order to use the individually-identifiable human biological material without appropriate consent in the next human biomedical research. Do note that the waiver of appropriate consent under the Act only applies to human biomedical research and not any other research.

Human Biomedical Research Compared with Clinical Trials Regulations

Q33: How will the Act affect future clinical drug trials and their sponsors?

Research projects that are clinical drug trials will continue to be regulated under the Clinical Trials Regulations administered by the Health Products Act or Medicines Act. While such clinical research dealing primarily with therapeutic products or medicines with therapeutic claims come under the scope of the Act, they will be formally exempted from the Human Biomedical Research Act and the Clinical Trials Regulations will continue to regulate such research.

Sponsors of clinical trials should continue to comply with the relevant requirements under the Clinical Trials Regulations.

The Clinical Trials Regulations and the Human Biomedical Research Act are complementary to each other and share the same principles of i) good ethical and clinical conduct of research requiring an approval by an institutional review board, ii) informed consent for the research subject's participation, iii) giving the individual the right to decide to participate or withdraw without penalty, and most importantly, iv) ensuring the safety and welfare of all research subjects.

Q34: Can a sponsor or funding body be a research institution?

Any entity such as a pharmaceutical company or a clinical research organisation (CRO) can be a research institution as long as it satisfies the responsibilities and obligations of a research institution as stipulated in the Act. If a sponsor or a funding body is able to fulfil the obligations, and wishes to establish itself as a research institution, it can submit a notification to HSA to establish itself as a research institution. It will then become subject to the regulatory requirements under the Act.

Scope of Human Tissue

Q35: Why are certain types of human biological material excluded from the definition of human tissue?

The Act does not seek to regulate any human tissue that are naturally excreted from the body such as bodily fluids and waste products such as saliva, sweat, urine and faeces. This also includes hair shaft, cut without dermal hair root or follicle, and nail plate, cut without underlying dermal tissue. For the avoidance of doubt, placenta is not considered naturally excreted waste product and the prohibition on the commercial trading of human tissue in the Act will apply.

In relation to the prohibition against tissue trading, it will be illegal to buy or sell human tissue in general, although it will be permissible to provide reimbursement for expenses "reasonably incurred" in relation to storage, processing, donation of tissue from the human body and associated healthcare and insurance costs. This prohibition aims to protect the safety and welfare of donors, ensure that donations of human tissue are altruistic in nature, and to maintain due respect for the human body.

Human tissue that have been de-identified and processed into a different state where their biological, structural and functional properties have been substantially manipulated as compared to the time of collection will not be prohibited from commercial trading. The rationale here is that once work and skill is applied to the tissue, there is the right to sell the tissue so processed for valuable consideration.

You may wish to use the Human Tissue Framework Decision Tool found here to find out whether you are handling human tissue under the Act.

Note:

The buying and selling of human organs and blood are prohibited under the Human Organ Transplant Act (HOTA). This prohibition (under HOTA) does not apply to products derived from blood that had been subjected to processing or treatment e.g. human blood plasma or serum.

The buying and selling of human oocytes, sperms and embryos are prohibited under the Human Cloning and Other Prohibited Practices Act (HCOPPA).

Q36: In relation to the prohibition against advertisement, does it mean that companies may not advertise their services on the internet? Does this apply to foreign companies who advertise in publications that are accessible in Singapore?

Yes. It will be an offence to advertise the purchase or sale in Singapore of human tissue as defined in the Act. This includes all forms of advertising, regardless of the national origin of the advertiser.

Regulation of Tissue Banking Activities

Q37: What are legacy human biological material?

Legacy human biological material refer to those that have been removed from a donor and rendered non-identifiable prior to the Human Tissue Framework coming into force on 1 November 2019.

For such human biological material, only the following sections of the Act would apply:

- section 30 on prohibited human biomedical research,
- section 31 on restricted human biomedical research,
- section 32 on prohibition against commercial trading of human tissue and
- section 33 on prohibition against advertisements relating to commercial trading of human tissue.

Q38: I am using non-identifiable human tissue for research. Do I need to be a tissue bank? How can I ensure appropriate consent is obtained for such tissue?

The use of non-identifiable human tissue for research is regulated under the Act. The requirements of the human tissue framework, including notifying as a tissue bank and obtaining appropriate consent for the tissue banking activity will apply regardless of whether the tissue is identifiable . This is to ensure that the autonomy of tissue donors is always respected when they donate their tissue for use in research.

Where non-identifiable tissue are obtained locally for research, the tissue bank should maintain documentation to show that appropriate consent had been obtained. This could be in the form of a redacted copy of the consent form signed by the tissue donor. Where the tissue are imported into Singapore, the tissue bank should obtain a declaration to show that consent had been obtained in accordance with the legal or ethical requirements of the place the tissue had been imported from.

Q39: Do I need a licence from HSA to operate as a research tissue bank?

Under the Act, research tissue banks will need to notify HSA of its operation through TIARAS with a one-time notification fee of $1,000. The research tissue bank can proceed to commence its first tissue banking activity 30 days after the submission of the notification to HSA. Notwithstanding, if the tissue bank is also handling tissue for therapeutic purposes, requirements under the Healthcare Services Act will apply.

Q40: When will I need to notify as a tissue bank under the Act?

You will need to notify as a tissue bank under the Act if you conduct tissue banking activities such as storage, collection, procurement, import, supply, provision or export of human tissue for the purposes of facilitating current or future research or for public health or epidemiological purposes. Exceptions include if the tissue banking activities are exempted under the Human Biomedical Research (Tissue Banking and

Notification – Exemption) Regulations 2019. Your involvement in these activities should be clearly stated in the protocol of the human biomedical research, clinical trial or national public health research, or in the form of service agreement for service providers contracted to support these activities.

For avoidance of doubt, you will need to notify as a tissue bank under the Act if you conduct tissue banking activities **beyond** the specific objectives and endpoint of the abovementioned exceptions e.g. storage/supply/export of leftover tissue from a clinical trial for future research.

You may refer to the TIARAS Screenshots for Notifications (Tissue Bank) for a step-by-step guide on how to notify as a tissue bank.

Q41: I am a contract research organisation or laboratory that is importing or collecting tissue to support clinical trials. Do I have to notify as a tissue bank?

If you are conducting tissue banking activities for clinical trials that are regulated under the Health Products Act or Medicines Act, you need not notify as a tissue bank under the Act. Your involvement in these activities should be clearly stated in the protocol or in the form of service agreement for service providers contracted to support these activities.

If you are conducting tissue banking activities for clinical trial activities that are not regulated under the Health Products Act or Medicines Act, you will need to notify as a tissue bank under the Act.

Q42: Do I need to apply for a permit to import human tissue for research purposes?

There is no permit requirement under the Act for the importation of human tissue. However, the importation of human tissue for research is a tissue banking activity that must conducted under the supervision of a tissue bank that has notified HSA.

Q43: I collect/import cadavers for the purposes of education and training. Do I need to be a tissue bank?

No, only tissue banking activities for the purposes of facilitating current or future research, public health or epidemiological purposes will need to be conducted under the supervision and control of a tissue bank.

Nonetheless, the prohibition against commercial trading of human tissue and advertisements relating to the commercial trading of human tissue (sections 32 and 33) of the Act and the corresponding prohibition for organs and blood under sections 14 and 15 of the Human Organ Transplant Act will apply.

Q44: Do I need to obtain approval from an institutional review board for the tissue banking activities conducted by my tissue bank?

No. Unlike the human biomedical research framework, tissue banks are not required to obtain approval from the institutional review board to conduct tissue banking activities under the Act.

Notwithstanding, Regulation 15 of the Human Biomedical Research (Tissue Banking) Regulations 2019 requires the tissue bank supplying tissue to any person for research to ensure that there is either approval from the institutional review board or scientific merit for the proposed research (for non-identifiable tissue), prior to the supply.

Q45: Is it permissible for tissue banks to supply tissue to a researcher for use in research (not to be exported), if the researcher is able to show that the institutional review board has exempted from review the proposed research that the tissue would be used for?

Yes, it is permissible for tissue banks to supply tissue to a researcher for use in research if the institutional review board had exempted from review the proposed research the tissue would be used for. However, the tissue bank must also ensure that there is documentary evidence that the intended use of the tissue is in accordance with any conditions or restrictions specified as part of the consent given by the donor.

Q46: Under what circumstances would a proposed research have scientific merit to allow tissue bank to supply the non-identifiable tissue for the purpose of research?

Generally, a proposed research would be regarded as having “scientific merit” if a group of scientific experts who have no part in the proposed research endorses the proposed research. Such endorsement may be by way of a letter awarding project grant(s), formal approval by an institution’s professional board or formal approval by an institution’s scientific experts.

Q47: Are tissue banks required to formulate a policy on any incidental findings in relation to tissue they have received for use in research?

Yes. Similar to the functions and duties of a research institution, tissue banks will be required to formulate an internal policy governing any incidental findings in relation to tissue they have received for use in research. The policy should cover if the tissue donor should be re-identified and informed, in the case of an incidental finding in relation to a tissue.

From 1 November 2019, tissue banks are required to inform all tissue donors and recipients of their incidental finding policy.

Consent for Tissue Donation

Q48: Would all future research use of tissue collected prior to implementation of the Human Tissue Framework be exempted from requirements of appropriate consent?

No. Any tissue collected before the activation of the Human Tissue Framework (on 1 November 2019) may only be used in future research if the donor's consent was obtained, unless the tissue has been rendered non-identifiable before the activation of the Human Tissue Framework (i.e. legacy human biological material). The elements of information under section 12(2)(a), 12(2)(f) and 12(2)(i) of the Act must be provided to the tissue donor before consent is obtained. In addition to this requirement, the use of the tissue must fall within the scope of consent provided.

Q49: Why must personal consent be obtained for the removal and use for research of certain tissue such as gametes (sperm and eggs) and embryos?

Where eggs, sperm and embryos are concerned, the ethical concerns surrounding the use of such tissue in research are often sensitive as they are closely related to procreation issues, and may have direct consequences to donors themselves. As such, the Act requires that the donor himself or herself be fully informed of the nature and consequences of the donation and that **personal consent** is obtained. Proxy consent for minors and for mentally incapacitated adults is invalid. This also means that legacy tissue that are sperms, eggs or embryos may not be used any further for research since it would not be possible to obtain personal consent.

Q50: Can donors change their mind on their original consent for how the donated tissue may be used or withdraw their consent?

Yes. Donors can change their mind on how their donated tissue are to be used as long as the tissue have not been de-identified. Donors may also withdraw consent for use of their tissue in research. If the tissue has already been used for research, the data already generated from that tissue remains part of the research and will not be removed. However, **prospective** data cannot be generated from that tissue upon the withdrawal of consent for its use. The Act's intent is that the donor's wishes be respected as far as possible.

Q51: Are imported tissue bound by the appropriate consent requirements stipulated by the Human Biomedical Research Act?

For imported human tissue, it is recognised that there will be practical difficulties in ensuring that the consent obtained overseas fulfils the prescribed requirements of appropriate consent as stipulated in the Act.

As such, the Act considers there to be sufficient compliance if there is documentary evidence that consent has been obtained in accordance with the legal or ethical requirements of the country where the tissue is imported from. There should also be documentary evidence that the human tissue was supplied on a cost-recovery basis, with no commercial trading involved, in line with section 32 of the Act.