

FAQs ON HUMAN BIOMEDICAL RESEARCH ACT

Q1: What are the objectives of the Act?

A: 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?

A: 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 will the Act be implemented?

A: MOH plans to have a 'sunrise period', the duration of which will be communicated later, to allow sufficient time for the affected parties to make the transition into the regulatory framework set out in the Act.

Scope of Human Biomedical Research

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

A: 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.

Q5: Are there any prohibited or restricted categories of human biomedical research?

A: 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 MOH. For such matters, MOH 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

Q6: What is the basis for prohibiting certain types of human biomedical research?

A: 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.

Q7: What is the basis for regulating human-animal combination research?

A: 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

Q8: Who are the key entities in this regulatory framework for human biomedical research? How do they relate to one another in this framework?

A: 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 enrolls 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.

Institutional Review Boards

Q9: What is an institutional review board? What is the role of the institutional review board in this regulatory framework?

A: 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.

Q10: What is the relationship between an institutional review board and a research institution?

A: 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.

Q11: What is the effect of the Act on existing institutional review boards?

A: Once the Act is enacted, the regulatory framework will only recognise institutional review boards that are appointed by a research institution. Other boards or committees that are not appointed by a research institution will not be considered as institutional review boards for the purposes of this Act.

Q12: Can a researcher whose project was rejected by one institutional review board seek a second review by another institutional review board?

A: 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.

Researchers

Q13: What is the relationship between a researcher and a research institution?

A: 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.

Q14: How will the Act affect researchers who are not affiliated with any research institution?

A: Currently, there may be some researchers who carry out human biomedical research on their own, and have no formal affiliation with any research institutions. Once the Act is enacted, and should that researcher wish to continue conducting human biomedical research, he or she would need to have the necessary contractual or other arrangement with a research institution. This is so that the proposed research can be conducted under the supervision and control of that research institution.

Q15: Will MOH be issuing licences for researchers to conduct research?

A: No, MOH 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.

Q16: 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?

A: 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 to the Act's requirements.

Research Institution

Q17: What is a research institution? What is the role of the research institution in this regulatory framework?

A: 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.

Q18: If today an organisation or entity has its own institutional review board, does it mean it is a research institution?

A: 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 MOH before it commences operation as a research institution. Subsequently, the organisation is required to submit a declaration of compliance to MOH 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.

Q19: Must the research institution be located in Singapore?

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

Q20: Can the research institution be located overseas and have a branch office in Singapore?

A: 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 MOH 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.

Q21: What is the effect of the Act on an organisation that has appointed and is presently supporting and maintaining its own institutional review board?

A: Once the Act takes effect, an organisation that currently supports its own institutional review board to conduct ethics reviews of human biomedical research, needs to decide if it would like to formally establish itself as a research institution. If it chooses not to, its institutional review board cannot continue to function as such.

Where by reason of the small size of the organisation or the small number of research proposals it is impractical to establish and maintain a standing institutional review board of its own, the organisation can make clear arrangements to collaborate with an established research institution, which would allow the research proposals to be considered by the institutional review board of that research Institution. Alternatively, it is permissible for several institutions jointly involved in the same research to jointly appoint a common institutional review board. However, each of these institutions must be prepared to take on the role and responsibilities of a research institution themselves.

The Act also does not preclude groups of research institutions arranging for one parent organisation to take on the role of research institution, and to appoint the necessary institutional review boards for its constituent institutions, for example, SingHealth on behalf of SGH.

Q22: Can a researcher be a research institution?

A: 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.

Scope of Human Tissue

Q23: Why are certain types of human biological material excluded from the definition of human tissue?

A: 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 in the Act on the commercial trading of human trading 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 or 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.

Q24: What are legacy tissue?

A: Legacy tissue are tissue that have been removed from a donor and rendered non-identifiable prior to the Act coming into force.

Regulation of Tissue Banking Activities

Q25: Why must personal consent be obtained for the removal and use for research of certain tissue such as gametes (sperm and eggs) and embryos?

A: 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.

Q26: Can donors change their mind or withdraw their original consent for how the donated tissue may be used, for example, in relation to consent restrictions?

A: Yes. Donors can change their mind or withdraw their consent on how their donated tissue are to be used as long as the tissue have not already been de-identified. If the tissue have already been used for research, 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 the consent for its use.

This does not contradict the fact that tissue donation should be an outright gift. The Act's intent is that the donor's wishes be respected as far as possible.

Q27: Are imported tissue bound by the appropriate consent requirements as stipulated by the Human Biomedical Research Act?

A: 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 came from.

Advertisement relating to the Buying and Selling of Human Tissue

Q28: 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?

A: 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.

Human Biomedical Research compared with Clinical Trials Regulations

Q29: How will the Act affect future clinical drug trials and their sponsors?

A: Research projects that are clinical drug trials will continue to be regulated under the Clinical Trials Regulations¹ administered by the HSA. 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.

Q30: Can a sponsor or funding body be a research institution?

A: 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 MOH to establish itself as a research institution. It will then become subject to the regulatory requirements under the Act.

Serious Adverse Events & Interventions by MOH

Q31: How does the Act deal with Serious Adverse Events? Under what circumstances will MOH intervene or put a stop to a research?

A: Under the Act, research institutions are required to report serious adverse events to MOH. Currently, the following are listed as being serious adverse events:

- a) in relation to human biomedical research, this means any untoward medical occurrence as a result of any human biomedical research which—
 - i) results in or contributes to death;
 - ii) is life-threatening;
 - iii) requires inpatient hospitalisation or prolongation of existing hospitalisation;
 - iv) results in or contributes to persistent or significant disability or incapacity;

¹ Currently the Medicines (Clinical Trials) Regulations under the Medicines Act, but will likely be 'ported over' to the Health Products (Clinical Trials) Regulations under the Health Products Act in the future.

- v) results in or contributes to a congenital anomaly or birth defect; or
 - vi) such other event as may be prescribed.
- b) in relation to tissue banking activity, this means any untoward occurrence associated with the procurement, testing, processing, storage or distribution of human tissue (including gametes or embryos) intended for human application which—
- i) results in or contributes to death;
 - ii) is life-threatening;
 - iii) requires inpatient hospitalisation or prolongation of existing hospitalisation;
 - iv) results in or contributes to persistent or significant disability or incapacity;
 - v) results in transmission of a communicable disease;
 - vi) results in any misidentification or mix-up of any type of tissue, gametes or embryo; or
 - vii) such other event as may be prescribed.

In the event MOH 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 Director of Medical Services 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.