FAQs on Human Tissue Framework

The Human Tissue Framework (HTF) is in operation since 1 Nov 2019. Tissue banking activities must be conducted under the supervision of a Tissue Bank that has notified MOH of its operations. Tissue banking activities conducted in industry sponsored clinical trials may also be subjected to HTF. Here are some Frequently Asked Questions from industry sponsors and CROs.

Update (11 Jan 2022): The HTF FAQ has been updated following our discussion with MOH to address tissue banking activities conducted for HSA regulated clinical trials. This update clarifies the instances where Health Products Act (HPA)/ Medicines Act (MA) will apply and HTF will not apply. This is to avoid dual regulations (both HPA/MA and HTF) for tissue banking activities. Updated information are shown in blue text.

For any queries relating to SingHealth Tissue Banks, please contact singhealthtissuebank@singhealth.com.sg.

No	Question	Answer
General		
1	What does a 'Tissue Bank' refers to? Is there a specific SingHealth Tissue Bank that sponsor can submit the future research ICFs to? Does it refer to any commercial/generic tissue banking facility selected by sponsor?	A "tissue bank" means an individual or a body of persons, whether corporate or unincorporate, or other organisation, that carries on or conducts any tissue banking activity but excludes an individual, a body of persons or an organisation that conducts any tissue banking activity solely for the purpose of the person's or organisation's own human biomedical research approved or exempted from review by an institutional review board. Tissue Bank activity refers to a structured and an organised 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: (a) the collection, storage, procurement or importation of human tissue; (b) the supply, provision or export of human tissue For more details, please refer to the definition under HBRA https://sso.agc.gov.sg/Act/HBRA2015. For the complete list of MOH registered Tissue Banks (including Tissue Banks in SingHealth) in Singapore, you may refer to list issued by MOH for information. https://www.moh.gov.sg/docs/librariesprovider5/legislation/tissue-banks-that-notified-moh-of-their-operations.pdf The SingHealth site should contact the appointed SingHealth Tissue Bank at their institution.

2	Could you provide more information on the application process to set up a Tissue Bank?	To set up a Research Tissue Bank in SingHealth, you may refer to SHS-RSH-ORIC-CWP-301, Formation and Cessation of Research Tissue Banks. You may also contact: singhealthtissuebank@singhealth.com.sg For others, you may refer to the MOH information: https://www.moh.gov.sg/docs/librariesprovider5/legislation/tiaras-screenshots-for---notifications-(tissue-bank)
3	Could you clarify what qualifies as future research vs. human tissues collected within the scope of the current HSA-approved clinical trial?	If human tissue samples are collected and stored solely for research to meet the objectives and endpoints described in the clinical trial protocol, this would be deemed to be within the scope of the HSA-approved clinical trial. The required amount of human tissues for the research will be stated clearly in the protocol. If human tissue samples are collected and stored for research that is unrelated to the study objectives and endpoints, or for unspecified future research, then such activities may be regulated under the Human Tissue Framework.
4	If the site has been registered as a Tissue Bank and the sponsor of the clinical trial wishes to store the human tissue samples in an overseas Tissue Bank, is this allowed?	If the involvement of the hospital/site performing the tissue banking activities is clearly documented e.g. in the Clinical Trial protocol or agreement, such that its tissue banking activities are conducted to meet the specific objectives and endpoints of the HSA-approved Clinical Trial protocol, the hospital/site does not need to be a TB under the Human Tissue Framework (HTF). These activities should be already regulated under the Health Products Act (HPA) or the Medicines Act (MA). This is to avoid dual regulation. However, if the tissue banking activities are not performed for the purpose of the HSA approved Clinical Trial protocol, for the tissue banking activities conducted in Singapore, the site can either setup as a research Tissue Bank or come under the oversight of a research Tissue Bank. For the tissue banking activities occurring at local site that is not performed for the purpose of HSA approved Clinical Trial protocol, the local MOH registered TB will need to be involved. This TB will be responsible for the collection, interim storage and transfer of human tissue to the overseas TB. Refer to Q15 – Q25 for HSA regulated Clinical Trials.

		A material transfer agreement or clinical trial agreement should address the arrangement between sponsor and site.
5	Must all human tissue samples collected for future research be transferred to a Tissue Bank before sending to the sponsor?	The human tissue samples are not required to be physically transferred to the Tissue Bank before sending to the sponsor. Refer to Q15 – Q25 for HSA regulated Clinical Trials for the collection of leftover or addition human tissues which may be subjected to HTF where a Tissue Bank oversight is required.
6	Does HTF apply since the sponsor only receive de-identified human tissues samples located overseas for the future research?	Tissue banking activities include collection of human tissues. The starting point is that the site team collects identifiable human tissues. If the involvement of the hospital/site performing the tissue banking activities is clearly documented e.g. in the Clinical Trial protocol or agreement, such that its tissue banking activities are conducted to meet the specific objectives and endpoints of the HSA-approved Clinical Trial protocol, the hospital/site does not need to be a TB under the Human Tissue Framework (HTF). These activities are already regulated under the Health Products Act (HPA) or the Medicines Act (MA). This is to avoid dual regulation. However, if the tissue banking activities are not performed for the purpose of the HSA approved Clinical Trial protocol, this will be subjected to the Human Tissue Framework (HTF). Refer to Q15 – Q25 for HSA regulated Clinical Trials.
7	Do I have to obtain consent from patients to use their de-identified human tissues for future research?	You will need to ensure that consent has been obtained in accordance to HBRA section 12(2) from the patients for future research.
8	May I know if IRB approval is required for the release of samples from a SingHealth Research Tissue Bank to tissue requestor?	It will depend on the purpose of the tissue request. 1. If the request is to retrieve identifiable samples for a new research, IRB approval is required. According to *HBRA Human Biomedical Research (Tissue Bank) Regulations 2019, Section 15(1) - Before any tissue which is individually-identifiable may be removed from the supervision and control of, or supplied by, a tissue bank to any person for use in research carried out by that person in circumstances other than in paragraph*

		(4), the tissue bank must ensure that — *(a) an institutional review board has approved or exempted from review the proposed research that the tissue would be used for and* *(b) there is documentary evidence provided by the recipient (such as but not limited to a letter of undertaking) to the effect that the recipient will ensure that the intended use of the tissue is in accordance with any conditions or restrictions specified part of the* ***appropriate consent of the donor.*** 2. If the request is to retrieve non-identifiable samples for secondary research, IRB review is not required. There should be sufficient justification that the Tissue Bank is satisfied that there is scientific merit for the proposed research. According to *HBRA Human Biomedical Research (Tissue Bank) Regulations 2019, Section 15(2) - Before any non-identifiable tissue may be removed from the supervision and control of or supplied by a tissue bank to any person for use in research carried out by that person, the tissue bank must ensure that —* *(a) either an institutional review board has approved or exempted from review 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* *(b) there is documentary evidence provided by the recipient (such as but not limited to a letter of undertaking) to the effect that the recipient will ensure that the intended use of the tissue is in accordance with any conditions or restrictions specified as part of the* ***appropriate consent of the donor****.*
9	In the RICE webinar held on 27 Jan 2021, slide 37 mentions that the TB holds the key and releases the de-identified samples to the researchers who requested the samples. If a researcher wants to retrieve identifiable samples from the SingHealth Research Tissue Bank, can that be done? This is assuming researcher will get IRB approval to use identifiable tissues for the research.	This will depend on the SingHealth Research Tissue Bank's Policy as some SingHealth Research Tissue Banks may only release non-identifiable information. Please note that IRB approval is required for the use of identifiable data/tissues for a research. IRB approval does not overwrite the Tissue Bank's Policy and the release of the samples will be in accordance to the Tissue Bank policy. You may want to check with the respective SingHealth Research Tissue Bank directly.
10	Consider a scenario where HBR is conducted using the tissue stored in Tissue Bank. If a subject has decided	It will depend on the process of the Tissue Bank as each Tissue Bank has its own policies and procedures. It will

	to withdraw from the HBR study, should the tissue stored in a tissue bank be discarded as well? Or the withdrawal of the subject from HBR is not related to the withdrawal of tissue from Tissue Bank?	also depend on what the subject has consented to in the Tissue Bank Consent form. If the subject has decided to withdraw from the donation, he/she should contact the Tissue Bank stated on the consent form and the Tissue Bank must carry out the necessary actions that were promised in the consent document and according to the Tissue Bank policy, e.g. if the Tissue Banking samples collected are released to a researcher conducting HBR, the Tissue Bank will inform the researcher to discontinue using the samples at their end.
11	Does the responsibility of HBRA and HTF fall on the Contract Research Organization (CRO) (i.e. testing lab CRO) or Sponsors (i.e. Pharma/Biotech companies)? Both the CRO and Sponsor do not own the specimens from patients.	It will depend on the role of the CRO testing lab. For example, if the CRO is a service provider that provides testing services, there should be an agreement in place with the Sponsors. If the CRO is the Tissue Bank responsible for the tissue banking activities, the CRO shall ensure that appropriate consent in accordance to HBRA Section 12(2) has been obtained for conducting of any tissue banking activities such as the removal, donation or use of tissues. Refer to Q15 – Q25 for HSA regulated Clinical Trials.
12	Will hospitals be considered as conducting tissue banking activities when it supplies human tissue?	Hospitals or pathology/clinical departments will be considered as conducting tissue banking activities if it involves human tissue for the proposes 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: a)the collection, storage, procurement or importation of human tissue; b)the supply, provision or export of human tissue. The primary role of a pathologist is to conduct clinical diagnosis. The pathology/clinical departments should work with the Tissue Bank to address the transfer of tissues from the pathology/clinical departments to the Tissue Bank before releasing to the researchers. Refer to Q15 – Q25 for HSA regulated Clinical Trials.
13	Who is the responsible party to ensure that appropriate consent had been taken obtained before the HBM and data could be used for research? Will it be the researcher collecting the tissue or the Tissue Bank or the researcher requesting for the tissues?	The person obtaining consent will be responsible for ensuring that appropriate consent (including presence of witness if not exempted) has been obtained in accordance with the HBRA Section 12 elements. The person should also ensure that an approved version of

		the consent form (approved by the IRB or Tissue Banking Committee/SBRSA) is used to obtain the consent. If the collection is carried out during a HBR or clinical trial, the authorized study team member of the HBR/clinical trial will be obtaining the consent from the research participant. If the collections are initiated by the Tissue Bank, the personnel authorized by the Tissue Bank will be obtaining consent from the donor. The Tissue Bank, or the person acting under the supervision of the Tissue Bank who is releasing the tissues for research is also responsible for ensuring that appropriate consent is in place before releasing the tissues.
14	For biospecimen obtained from overseas bank/ non-commercial sources, is IRB review required if the biospecimen is de-identified?	IRB review is not required for obtaining de-identified tissue from overseas bank/non-commercial sources. The transfer of samples from one entity to another is under the oversight of the institution. However there should be proper documentation of the transfer e.g. Material Transfer Agreement.
Human Tissue samples collected for current HSA-approved Clinical Trial		
15	In Clinical Trials regulated by HSA, is the exemption from HTF only applicable to the conduct of tissue banking activities for the investigator's own approved clinical trial and not for future research?	For the conduct of tissue banking activities (e.g. collection of tissues) for the purpose of the investigator's own HSA-approved clinical trial (under HPA/MA), it will be exempted from the HTF. When the tissue samples are collected and stored solely for research to meet the objectives and endpoints described in the clinical trial protocol, this would be deemed to be within the scope of the HSA-approved clinical trial. The human tissues do not need to be stored in a Tissue Bank. The investigator should manage the collected tissues as described in the protocol and informed consent document, e.g. the collected human tissues will be destroyed at study completion.
16	**(NEW)** In Clinical Trials regulated by HSA, when leftover diagnostic human tissues are obtained from hospitals **for the purpose of the current approved clinical trial**, does the hospital need to be a Tissue Bank?	The tissue banking activities are performed under the current approved clinical trial such that these activities are regulated under the Health Products Act (HPA) or Medicines Act (MA). In this case, it is not required for the hospital to be a Tissue Bank. The Human Tissue Framework (HTF) does not apply for the tissue banking activities done according to the approved clinical trial protocol which is already

		subjected to the HPA/MA. This is to avoid dual regulation. However, tracking of the tissue released should be properly documented. If the tissue banking activities conducted are no longer under the scope of HPA/MA, the HTF will apply and a Tissue Bank is required.
17	In a study, human tissues samples collected for biomarker testing will be used for the purposes described in the study procedures section and will be destroyed at the end of their usable life or the end of the scheduled storage period. During the course of the study, the human tissue samples will be stored in an overseas Tissue Bank. Do we need to comply with HTF?	When the tissue samples are collected and stored overseas solely for research to meet the objectives and endpoints described in the clinical trial protocol, this would be deemed to be within the scope of the HSA-approved clinical trial. This will not be regulated under HTF. Furthermore, the human tissue samples will be destroyed at end of their usable life or end of scheduled storage. A material transfer agreement or clinical trial agreement should address the arrangement between sponsor and site.
Use of Leftover Human Tissue samples for Future Research		
18	**(NEW)** In Clinical Trials regulated by HSA, human tissues are **collected as part of the approved clinical trial** where leftovers human tissue will **subsequently be used for future research in overseas.** There could be a **short term storage (ie. batch shipping) in Singapore (at site or at the CRO/sponsor)** before the tissues are sent overseas for the current research, does the site or CRO/sponsor need to be a Tissue Bank?	For storage or export of Human Tissues for the purpose of a HSA-approved clinical trial, it will be regulated under the Health Products Act (HPA) or Medicines Act (MA). The Human Tissue Framework (HTF) does not apply for the tissue banking activities (ie. short term storage) performed according to the approved the clinical trial protocol which is already subjected to the HPA/MA. This is to avoid dual regulation. Subsequently, the storage of leftover Human Tissue in overseas for future research will not be regulated as HTF does not have overseas jurisdiction. If the human tissues are sent overseas straightaway for the purpose of a HSA-approved clinical trial and have the left over tissues stored for future research, the storage of leftover Human Tissue in overseas for future research will not be regulated as HTF does not have overseas jurisdiction.
19	**(NEW)** In Clinical Trials regulated by HSA, human tissues are **collected as part of the approved clinical trial** where the left over human tissue will **subsequently be used for future research.**	When the tissue banking activities conducted to meet the specific objectives and endpoints of the HSA-approved clinical trial protocol are completed, HPA/MA will no longer regulate any further future research activities. Thus, the tissue banking activities for future research (e.g.

	At the interim, the left over human tissue are **stored in Singapore** to be used for future research. Does the site or CRO/sponsor need to be a Tissue Bank?	storage of leftover Human Tissues in Singapore) will be regulated under HTF and the activities must be conducted under the oversight of a MOH-registered TB.
20	If my biorepository is not a MOH-registered Tissue Bank, can we store the leftover human tissue samples collected from approved ongoing studies in the biorepository?	Any biorepository that is performing tissue banking activities (e.g. collection, storage, procurement, importation or supply) within Singapore must register with MOH as a Tissue Bank. You will not be able to supply leftover human tissue samples for other purposes that is not within the scope of the current clinical trial if you are not a Tissue Bank in Singapore. For more information, please refer to the resources below: https://sso.agc.gov.sg/SL/HBRA2015-S702-2019?DocDate=20191021 https://www.moh.gov.sg/docs/librariesprovider5/legislation/overview-of-human-tissue-framework.pdf
21	For current approved Clinical Trials that have stated the use of leftover HBM for future research in the consent form, but the consent form does not contain negative statements of elements that are not applicable. As most of the participants have passed on, it is not feasible to obtain consent even if there is an updated consent form containing all elements. How do we move forward to use the leftovers for future research?	For the collected human tissues which are planned to be used in future research, the HTF requirements will apply for human tissues collected after 1 Nov 2019 (HTF activation date). All the consent elements under HBRA Section 12(2) must be met. For human tissues collected before the HTF activation date (1 Nov 2019), MOH has granted an exception on this. You may want to check if the consent taken has met the minimum core elements for appropriate consent. For more details, please refer to the appropriate consent guidance document by MOH. https://www.moh.gov.sg/docs/librariesprovider5/legislation/guidance-on-appropriate-consent_17-may-2019.pdf
22	If a researcher has IRB approval for a HBR using leftovers human tissue (where consent is obtained from a previous HBR under the same researcher) for future research, what if there is a gap in the IRB approval of the 2nd HBR? Do the leftover human tissue (from the first HBR) need to go into a TB first?	Research and transfer of the leftover human tissue should only commence after you have received IRB approval for the 2nd HBR. Should there be a "gap" period, this duration will be subjected to HTF thus a Tissue Bank is required. You may retain leftover human tissue without going through a Tissue Bank if there are no gap between the

		studies and you are only transferring to your own research. For other research, the transfer or distribution of the leftover human tissue must be through a Tissue Bank. If there is no plan on a 2nd HBR after the 1st HBR has expired, human tissue have to be transferred to a Tissue Bank.
23	If leftover human tissue from a previous research to be used for future research, but the PI no longer acts as PI (e.g. as Co-I or becomes a collaborator) for the future research, is this considered as the researcher's own future research?	Whether it is considered as "own future research" will depend if the Co-I has any direct role in the study. For example, if the Co-I is involved in the recruitment and obtaining consent from the subject. A mere contribution of human biological materials to a study or an individual who received human biological materials is not considered as a study team member unless the individual is directly involved in the research study. Such transfers of human biological materials should be more appropriately documented in other documents such as a Material Transfer Agreement (MTA).
24	For the conduct of the researcher's own future research, does the current PI needs to be a PI for the next study? Or can he/she be a study team member to use the additional or leftover samples for the future research?	Whether it is considered as "own future research" will depend if the researcher has any direct role in the study. For example, if the researcher is involved in the recruitment and obtaining consent from the subject. A mere contribution of human biological materials to a study or an individual who received human biological materials is not considered as a study team member unless the individual is directly involved in the research study. Such transfers of human biological materials should be more appropriately documented in other documents such as a Material Transfer Agreement (MTA).
Collection of Additional/ Extra Tissues for Future Research		
25	In an industry sponsored clinical trial, the research site will export human tissue to an overseas repository and additional/extra human tissues may be kept for future research. The sponsor is not keen to register themselves as a Tissue Bank. How can the site carry out the tissue banking activities?	The site can collaborate with MOH registered TBs to supervise the conduct of the TB activities that the Sponsor may be involved in (e.g. human tissue samples collection, interim storage and export). The supervising TB will have to ensure that consent form meets the requirements set out in Part 3 and section 12(2) of the HBRA. In addition, the supervising TB will

		need to ensure all tissue banking activities are carried out in compliance with the HBRA/HTF requirements.
Informed Consent Form		
26	In a Clinical Trial regulated by HSA: - Main study ICF: Subject will provide consent for their collected human tissue samples to be used for future research. - Separate future research ICF: Subject will provide consent for future research. Is it required to remove the section for future research from the main ICF and remove the separate future research ICF from the CIRB application?	If the human tissue samples used for future research are leftover human tissue samples collected within the scope of current research, the section on the use of leftover for future research should be in a separate section from the main ICF. The future research consent section should include HBRA section 12 (2) elements. For the additional collection indicated in the future research ICF, this will be a separate consent and need not be submitted to CIRB. However such additional collection should be performed under a Tissue Bank oversight and the future research ICF must fulfil the HBRA section 12(2) elements. It is important to address the Tissue Bank information and HBRA 12(2) requirement in the consent form. For example: • Where will the human tissue be donated to • Storage of the human tissue for future research • Appropriate contact information according to Section 12 (2) (p): the person or persons to contact to obtain further information on the purposes for which the tissue will be used and to provide feedback in relation to such purposes, respectively.
27	For the conduct of my Tissue Banking activities, I will be approaching the existing Tissue Banks and come under the oversight of the existing MOH-registered Tissue Bank. Since the broad consent form from the Tissue Bank will be used, is it still required to submit the consent form for additional/leftover human tissue to CIRB?	This consent form can be attached as part of CIRB application submission but CIRB will not be approving this broad consent form from the Tissue Bank. You may use the approved SingHealth Research Tissue Bank consent form, with approval from the Tissue bank, where relevant for your collection. The PIs should have some agreement/documentation to indicate an arrangement has been made with the Research Tissue Bank and that the Research Tissue Bank is aware of this planned collection.
28	Collection of human tissue samples for future research should be conducted under the oversight of a Tissue Bank and using the Tissue Bank's consent form. Should the study team use the Broad consent form from the	The broad consent form from the Tissue Bank can be used, with approval from Tissue Bank, where relevant for your collection.

	Tissue Bank and submit to the Tissue Bank for approval instead of CIRB?	This broad consent form can be attached as part of CIRB application submission but CIRB will not be approving this broad consent form.
29	Since the HTF regulation does not apply outside of Singapore, who should the study team submit the future research ICFs for review?	In the case of leftovers human tissue samples collected within the scope of the study that will be used for future research, the future research consent for use of leftover human tissue samples should be submitted together with the HBR/CT application to IRB. In the case of additional human tissue samples collected for future research and not for the proposed research, this activity should be under the oversight of TB for the collection, interim storage and transfer of the human tissues. In this case the TB's consent document can be used with approval from the Tissue Bank, where relevant for your collection. This will not be required to be submitted to CIRB. For both scenarios involving leftover or additional human tissues, please ensure that consent has been obtained in accordance to HBRA section 12(2) from the patients for future research. A material transfer agreement or clinical trial agreement should address the arrangement on the use of human tissues between sponsor and site.
30	If my main study does not have any more active patients and all patients have been rolled over to the extension study, do I have to update the extension study or the main study for the additional/extra human tissue collection?	It's important to check if consent form that was used for the human tissue collected at that time meet the HTF requirements. For the collected human tissues which you plan to use in future research, the HTF requirements will apply for human tissue collected after 1 Nov 2019 (HTF activation date). The consent requirements for HBRA section 12(2) must be met. For human tissues collected before the HTF activation date (1 Nov 2019), you may want to check if you have met the minimum core elements for appropriate consent. For more details, please refer to the appropriate consent guidance document by MOH. https://www.moh.gov.sg/docs/librariesprovider5/legislation/guidance-on-appropriate-consent_17-may-2019.pdf

31	Does collection of tissue banking samples require IRB approval? Or can we simply use the Informed Consent Form straightaway?	Collection of samples for tissue banking purposes falls outside the purview of CIRB. Tissue banking samples (including the use of the Informed Consent Form) will require approval from the respective Tissue Bank and/or SingHealth Biobank Research Scientific Advisory (SBRSA) Executive Committee. When an Informed Consent Form from a Tissue Bank is to be used, approval from the Tissue Bank is required as the samples are deemed as donated to the Tissue Bank and the Tissue Bank is the custodian of the samples.
32	Please provide some examples of how Section 12(2) element (b) and (c) can be shown on the ICF? If the elements are not applicable, is a negative statement required?	Some examples are as follows but are not exhaustive. The statements have to written within the context of your collection. For HBRA Section 12(2)(b), “whether the tissue will be used for any purpose other than research and if so, the specific purpose for which the tissue will be used”, you will need to clearly specify in the consent form the “use in future research” if the tissue will be used in future research. If there are no other purpose other than research, please state that the samples will only be used for the current research and specify the types of research (e.g. specific disease/ research area). For HBRA Section 12(2)(c), “the proposed areas of research approved by the institutional review board in a case where it has waived the requirement that the removal of the tissue is primarily for a therapeutic or diagnostic purpose under section 37(3)”, you may consider stating "The removal of the tissue involves no more than minimal risk and the research could not be carried out without the removal of the tissue". The IRB will review the proposed area of research involving these tissues. It is important to note that all HBRA Section 12(2) elements must be included in the informed consent form and to check your consent form after you have completed the customization to prevent accidental deletion of statements.