Guidance on the Requirement of Appropriate Consent for the Conduct of Human Biomedical Research and Handling of Human Tissue

Human Biomedical Research Act

Version as of 1 November 2026

Preface

The purpose of this document is to provide guidance to Research Institutions (RIs), Institutional Review Boards (IRBs), Tissue Banks (TBs) and researchers on the consent obligation for the conduct of human biomedical research (HBR) and handling of human tissue under the Human Biomedical Research Act (HBRA). In particular, this guidance addresses the consent requirements for the following existing activities:

1. HBR involving the use of individually-identifiable health information (HI) or individually-identifiable human biological material (HBM) without intervention;
2. HBR involving subjecting the research subject to any intervention; and
3. Storage, supply and use of human tissue collected before 1 November 2019.

The Health Sciences Authority (HSA) understands that most of the consent forms used by researchers for the ongoing HBR studies may contain a majority, but not the full list of the information elements as required in section 12 of the HBRA. As such, a balanced approach is adopted to allow the existing studies involving the use of HI or HBM to continue without the need to re-consent, so long as the minimal requisite set of "core" (and "situational", where relevant) information elements has been provided to the research subjects and that the studies had commenced prior to 1 November 2018. This approach ensures the continuity of such studies, whilst not compromising the safety and welfare of the research subjects recruited prior to the appointed date of the HBRA.

It should be noted that the information provided in this document only serves to advise on particular aspects of the HBRA, and is not meant to exhaustively address every obligation in the Act that would apply for the conduct of HBR or research tissue banking activities. For a more complete understanding of the requirements of the HBRA, this document should be read in conjunction with the Act and its Regulations.

If you need specific legal or professional advice, you should consult your research or legal offices or any other relevant professional advisors. Further, in the event of any contradictions between the contents of this document and any written law, the latter should take precedence.

CONTACT INFORMATION

Health Sciences Authority

Email: HSA_HBR_Enquiries@hsa.gov.sg

Website: https://www.hsa.gov.sg/human-biomedical-research/

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1. Appropriate consent under the HBRA

Under the Human Biomedical Research Act (HBRA), 'appropriate consent' must be obtained for the conduct of (1) HBR[1] and (2) handling of human tissue for research[2]. In general, 'appropriate consent' must be obtained:

a. in writing (which may be in electronic or other form of documentary evidence);
b. from the research subject or tissue donor personally or their legal proxy[3];
c. after all information referred to in section 12 of the HBRA[4] has been provided [except subsections 12(1)(e), 12(1)(j) and 12(2)(k) which should be provided only where applicable to the proposed study or tissue donation] and explained to the research subject or tissue donor or the legal proxy; and
d. in the presence of a witness.

❖ **How should appropriate consent be obtained and documented?**

Consent may be documented in a number of different ways. In general, appropriate consent should be obtained in writing, which is recorded in a manner that is accessible for future reference. It should also contain proof that appropriate consent had been obtained. Besides the usual hardcopy consent form that will contain the information and signature of the research subject or tissue donor, other examples could include video recordings and having the digital signature of the research subject or tissue donor printed on an electronic consent (e-Consent) form.

Where it is not practicable for the researcher to obtain consent through a physical face-to-face interaction with the research subject, the researcher may consider obtaining consent remotely, including phone calls, email correspondence followed by e-Consent, before commencing the research. For example, the researcher may:

a. send a recruitment letter to the research subject's residential address or personal email; or

[1] See HBRA section 3 for definition of "Human Biomedical Research".
[2] Handling of human tissue involves removal, storage, supply and use of tissue in research.
[3] Appropriate consent must be obtained from the legal proxies for persons who are unable to give personal consent, i.e. minors, persons who are mentally incapacitated or deceased. The hierarchy of respective legal proxies are listed under sections 7 to 11 of the HBRA.
[4] Section 12(1) contains the information elements that need to be provided to research subjects; section 12(2) contains the information elements that need to be provided to tissue donors.

b. call for participation and register subject's consent via an online portal.

In both cases, the information as required under section 12(1) of the HBRA should be clearly provided and it would be prudent to require the research subject's signature or digital signature (and the witness's signature for HBR involving interventions) to be returned to prove that consent had been obtained in cases of dispute.

Consent does not need to be obtained in the presence of a witness where:

a. the research is not interventional, not invasive and not restricted HBR[5]; or
b. the consent was obtained prior to 1 November 2017[6]; or
c. the human tissue is removed primarily for a therapeutic or diagnostic purpose

❖ **When is research considered interventional or invasive?**

- Research is considered <u>interventional</u> if it involves any activities that has a physical, mental or physiological effect (whether temporary or permanent) on the body of the research subject. Examples of intervention include (but are not limited to) buccal swabs, drawing of blood[7], X-ray or MRI scans.
- Research is considered <u>invasive</u> if it involves any procedure that is incisional, i.e. cutting into the tissue of the body. Examples of invasive procedures include (but are not limited to) finger-prick blood test and skin-prick test.

N.B. A study is not considered interventional (nor invasive) if the intervention is carried out primarily for **<u>non-research purposes</u>** (e.g. buccal swabs to collect cheek cells for diagnostic purposes). Similarly, research that comprises solely of a survey or collection of information from the research subjects is treated as not invasive and not interventional.

[5] See HBRA Fourth Schedule for list of restricted HBR.
[6] While the requirement for a witness is exempted if the consent is taken prior to 1 November 2017, this exemption will not apply if there are ongoing intervention after 1 November 2017 even for subjects recruited before 1 Nov 2017. In such cases, re-consent is still required at the next point of intervention and consent must be obtained in the presence of a witness.
[7] Where blood is drawn for the sole purpose of research or where excess blood is drawn beyond the amount required for clinical or diagnostic use, for research purposes.

2. Requirement of consent for conduct of existing HBR

2.1 HBR involving the use of individually-identifiable HI and/or HBM (**without** any further intervention[8])

2.1.1 For studies that commenced[9] before 1 November 2018

Unless the Institutional Review Board (IRB) has waived the requirement for appropriate consent, researchers must ensure that **the following seven mandatory "core elements" of information from section 12(1) have been provided to the research subject:**

- 12(1)(a) **investigational nature** of the research;
- 12(1)(b) **purpose** of the research;
- 12(1)(c) reasonably foreseeable **risks**, discomforts or inconveniences to the research subject arising from the research;
- 12(1)(d) **benefits** which the research subject may reasonably expect from the research;
- 12(1)(h) the extent to which **information identifying the research subject** will be kept **confidential**;
- 12(1)(k) whether the participation of the research subject involves information in **individually-identifiable** form; and
- 12(1)(n) the research subject's **right to withdraw** his or her consent and the limitations of such withdrawal from the research.

These elements are identified as **"core"**, as they are essential information that should be provided to all research subjects to ensure that their safety and welfare are being protected if they want to participate in an HBR.

As long as these seven core elements above have been provided to the research subject in the HBR which commenced before 1 November 2018, researcher may continue to:

[8] This may refer to studies in which there were interventions performed prior to 1 November 2018 but have no further interventions subsequent to 1 November 2018.
[9] This refers to the date that the study was approved by an IRB.

a. Recruit new research subjects till 31 October 2019, beyond which any new subject can only be recruited after all elements of information under section 12(1) have been provided;
b. Collect new HI and/or HBM[10] from the subjects recruited before 31 October 2019, provided that the collection of the HI or HBM is within the scope of IRB approval granted and the consent obtained; and
c. Use the HI and/or HBM collected in the current HBR.

Elements that are not listed above are considered "**situational elements**". Situational elements refer to those which should be communicated to the research subject if they are relevant to the research. If the "situational" elements had not been communicated to the research subject, then the said activity covered should not be conducted. For example, if the consent form did not mention the return of incidental findings (IFs), then researchers should not re-identify research subjects for the return of IFs, unless the subjects' consent to be re-identified for such a purpose was obtained prior to the re-identification. Similarly, the collected HI or HBM may only be used in a future HBR if the subjects had consented for their use in future research [as per 12(1)(i) and 12(1)(j) of the HBRA].

The full list of "core" and "situational" elements in section 12(1) can be found in **Annex A1**.

In the event where the study requires additional collection and use of individually-identifiable HI and/or HBM beyond the scope of research approved by an IRB and the consent obtained from the research subject, re-consenting[11] with all information elements under section 12(1) will be required. For example, in a study where the IRB has only approved the collection and analysis of full blood count but the researcher needs to analyse other biomarkers such as HbA1c, which goes beyond the scope of study approved by the IRB and the consent obtained, the researcher would need to seek IRB approval for the protocol amendment and to re-consent with all

[10] This collection does not include removal of tissue from the research subject for the purpose of the study, which would be considered an interventional HBR. An example of such collection could be obtaining the leftover tissue from the tissue repository after the diagnosis or therapy is completed. "Collection" is also generally considered to be a separate activity from "use".
[11] Re-consent is only required from the subjects who will be affected by the change of protocol, i.e. those who have completed the study and do not require additional HI and/or HBM to be collected do not need to be re-consented.

elements under section 12(1) for the research subject(s) that require the additional biomarkers to be analysed.

> ❖ **Do I have to use the exact wording of the consent elements under section 12?**
>
> To facilitate the research subject's ease of understanding, the consent elements may be paraphrased in layman's terms without following the exact wording of the provisions in the Act, so long as the intent of these elements had been communicated to the subject.

In non-interventional studies where individually-identifiable HI and HBM was obtained[12] before 1 November 2018 **without the core elements listed above**, researchers may continue to use the HI and/or HBM until 31 October 2019 under the following conditions[13]:

a. where there is documentary evidence that the research subject has given consent[14] before 1 November 2018 for the use of his or her individually-identifiable HI and/or HBM; and
b. the consent has not been withdrawn.

These studies are exempted from the appropriate consent requirements under the HBR (Exemption) Regulations released on 31 October 2018. For such HBR studies where the individually-identifiable HI and/or HBM will continue to be used beyond 31 October 2019, researchers should consider one of the following courses of action:

a. **obtain appropriate consent with all elements** listed under section 12(1);
b. **seek a waiver of consent** from the IRB in accordance with the conditions stipulated under the Fifth Schedule of the HBRA; or
c. **use** the HI and/or HBM in a **non-identifiable** form[15].

[12] This refers to when the HI and/or HBM was obtained from the research subject, either by the researcher directly for research or by the RI for a non-research purpose, e.g. HI and/or HBM was already obtained by the institution for diagnostic purposes.
[13] For avoidance of doubt, the exemption of appropriate consent for HBR does not apply to those which involve any intervention.
[14] This refers to the consent given by the research subjects in the absence of 'core' elements of information being provided.
[15] Use of non-identifiable HI and/or HBM does not require appropriate consent under the HBR framework. For the research to fall out of scope of the HBR framework, an "effective barrier" should be established

To better guide researchers in determining the necessary steps that need to be performed to continue their HBR, please refer to the flowchart in **Figure 1**.

2.1.2 For studies that commenced on or after 1 November 2018

Where the HI and/or HBM was obtained before 1 November 2018, researchers may use the HI and/or HBM so long as the core elements of information have been communicated to the research subject before his or her consent was obtained, unless the IRB has waived the requirement of appropriate consent.

Where the HI and/or HBM was obtained on or after 1 November 2018, researchers must ensure that **ALL elements** listed under section 12(1) of the HBRA (listed in **Annex A1**) have been provided to the research subject, before the subject's consent is obtained. Even when there is no intention by the researcher to carry out certain activities covered under section 12(1) (e.g. incidental findings will not be returned), the negative fact should still be conveyed to the research subject during the taking of appropriate consent, except for those indicated as "where applicable", i.e. section 12(1)(e), 12(1)(j), which can be omitted entirely if it is not applicable to the study.

2.1.3 Reporting of contravention for studies involving the use of individually-identifiable HI or HBM (without any further intervention)

Any HBR which commenced on or after 1 November 2018 involving only the use of individually-identifiable HI and/or HBM collected on or after 1 November 2018 that did not fulfil the requirements of appropriate consent, including providing the full list of consent elements, would need to be reported through the RI, to HSA as a contravention under the HBRA. For such studies, researchers have until **31 October 2019** to:

a. **seek re-consent** from the recruited subjects after the missing elements under section 12(1) have been communicated**;**
b. **seek a waiver of consent** from the IRB in accordance with the conditions stipulated under the Fifth Schedule of the HBRA; or

between the researcher using the de-identified HI and/or HBM and the person holding the re-identification key to minimise the risk of re-identification without consent.

c. **use** the HI and/or HBM in a **non-identifiable** form.

2.2 HBR involving **ongoing intervention beyond 1 November 2018**

2.2.1 Core elements and relevant situational elements were communicated

As any HBR would by default need to comply with all requirements of the HBRA from 1 November 2018, all elements under section 12(1) (listed in **Annex A1** for reference) of the HBRA should be provided to the research subject to fulfil the requirements of appropriate consent. **For HBR involving ongoing intervention where the full list of elements was not provided in the consent obtained, re-consent with the full set of elements under section 12(1) would be required.** As a practical approach to facilitate such studies, re-consent may be sought from the research subject **at the subject's next visit or before the next intervention**, as long as the list of "core" consent elements (outlined in section 2.1.1 of this guide) and the following situational elements relevant to interventional studies have been provided:

- 12(1)(e) where applicable, whether there are any alternative procedures or treatments available to the research subject, and the potential benefits and risks of such alternatives;
- 12(1)(f) any compensation and treatment available to the research subject in the event of injury arising from participation in the research; and
- 12(1)(g) any anticipated expenses the research subject is likely to incur as a consequence of participating in the biomedical research.

2.2.2 Core elements and relevant situational elements were not communicated

On the other hand, if the list of core and relevant situational elements (as above) have not been provided in the consent to the research subjects, re-consent from the recruited subjects would be required by providing the missing consent elements to the research subject. This re-consent would have to be conducted **before 1 November 2019, in order for the HBR study to continue.** This is in contrast to the timelines in the prior paragraph where re-consent could be taken at the research subject's next visit or intervention, as the core elements and relevant situational elements of the consent have **not** been communicated to the research subjects.

2.2.3 Reporting of contravention for studies involving ongoing intervention

For studies that commenced on or after 1 November 2018 in which the consent was obtained without providing the research subjects all the information elements under section 12(1) or where consent was obtained in the absence of a witness, they would need to be reported through the RI, to HSA as a contravention under the HBRA. The researchers will need to rectify the missing elements or missing witness at the subject's next visit or before the next intervention.

Where the list of core elements and the relevant situational elements have not been provided in the consent obtained, the study[16] would also need to be reported, through the RI, to HSA as a contravention under the HBRA. Re-consent from the recruited subjects would be required after the missing consent elements have been provided to the research subject **before 1 November 2019 to continue the HBR study**.

If there are no further interventions to the research subjects on or after 1 November 2018, the study would then be considered to be using only HI and/or HBM. In this regard, please refer to section 2.1 of this guide for information on the consent requirements.

[16] This would be regardless of study commencement date.

❖ **Summary of when re-consenting is required**

Re-consenting of research subjects required for studies involving the use of HI and/or HBM (without any further intervention)

Re-consenting of recruited subjects with all information elements under section 12(1) is required to continue the existing HBR[17] under the following circumstances:

a. For HBR which commenced **before 1 November 2018** where the core elements of consent were not provided to the research subject, researchers have up till 31 October 2019 to re-consent to continue the HBR;
b. For HBR which commenced **on or after 1 November 2018** involving only the use of individually-identifiable HI and/or HBM collected **on or after 1 November 2018** where the full list of consent elements under section 12(1) of the HBRA was not provided to the research subject, researchers have up till 31 October 2019 to re-consent to continue the HBR; or
c. For any HBR which requires collection and use of a new type of or additional HI and/or HBM that is **beyond the scope of research approved by an IRB and the consent obtained,** re-consent is required. However, researchers should seek also IRB's approval before re-consent to continue the HBR.

Re-consenting of research subjects required for HBR involving ongoing intervention

Re-consenting of recruited subjects with all information elements under section 12(1) is required, in the presence of a witness where applicable[18], to continue the existing HBR under the following circumstances:

a. Where the list of core and situational elements relevant to interventional studies **has not been provided** to the research subject, re-consent must be obtained on or before 31 October 2019 to continue the study;
b. Where the list of core and situational elements relevant to interventional studies has been provided to the research subject, re-consent must be obtained at the subject's next visit or before the next intervention;
c. Where the consent is not obtained in the presence of a witness [17], re-consent must be obtained in the presence of a witness at the subject's next visit or before the next intervention; or
d. For any HBR which requires a new form of intervention to be administered that is **beyond the scope of research approved by an IRB and the existing**

consent obtained, re-consent is required. However, researchers should seek also IRB's approval before re-consent to continue the HBR.

2.3 Seeking re-consent from research subjects

2.3.1 Missing consent elements

Where there are missing consent elements, researchers are only required to furnish the research subject with information on the missing elements during re-consent. There should also be documentation (e.g. signature) by the research subject to acknowledge that they have understood the additional information provided and that they agree to continue participating in the research in view of the new information.

Where the study involves ongoing intervention, a witness should also be present during re-consent to ensure that the subject is not coerced into continuing participating in the study.

2.3.2 Missing witness requirement

Where the consent was not obtained in the presence of a witness for HBR involving ongoing intervention, researchers are required to provide all elements in section 12(1) to the research subject at the subject's next visit or before the next intervention in the presence of a witness. The research subject and the witness' signatories should be properly documented to confirm the subject's voluntary participation in the study.

The role of the witness is to ascertain the identity of the subject giving the appropriate consent and that the consent was given voluntarily without any coercion or intimidation. However, HBRA does not require an impartial witness. Witness could be anyone 21 years old and above, including the study team member, member of the care team or the subject's family member. Nevertheless, this does not preclude institutions from adopting a higher standard for certain situations, such as where the subject is vulnerable or illiterate, or where the IRB deems that having an impartial witness is necessary to protect the safety and welfare of the research subject.

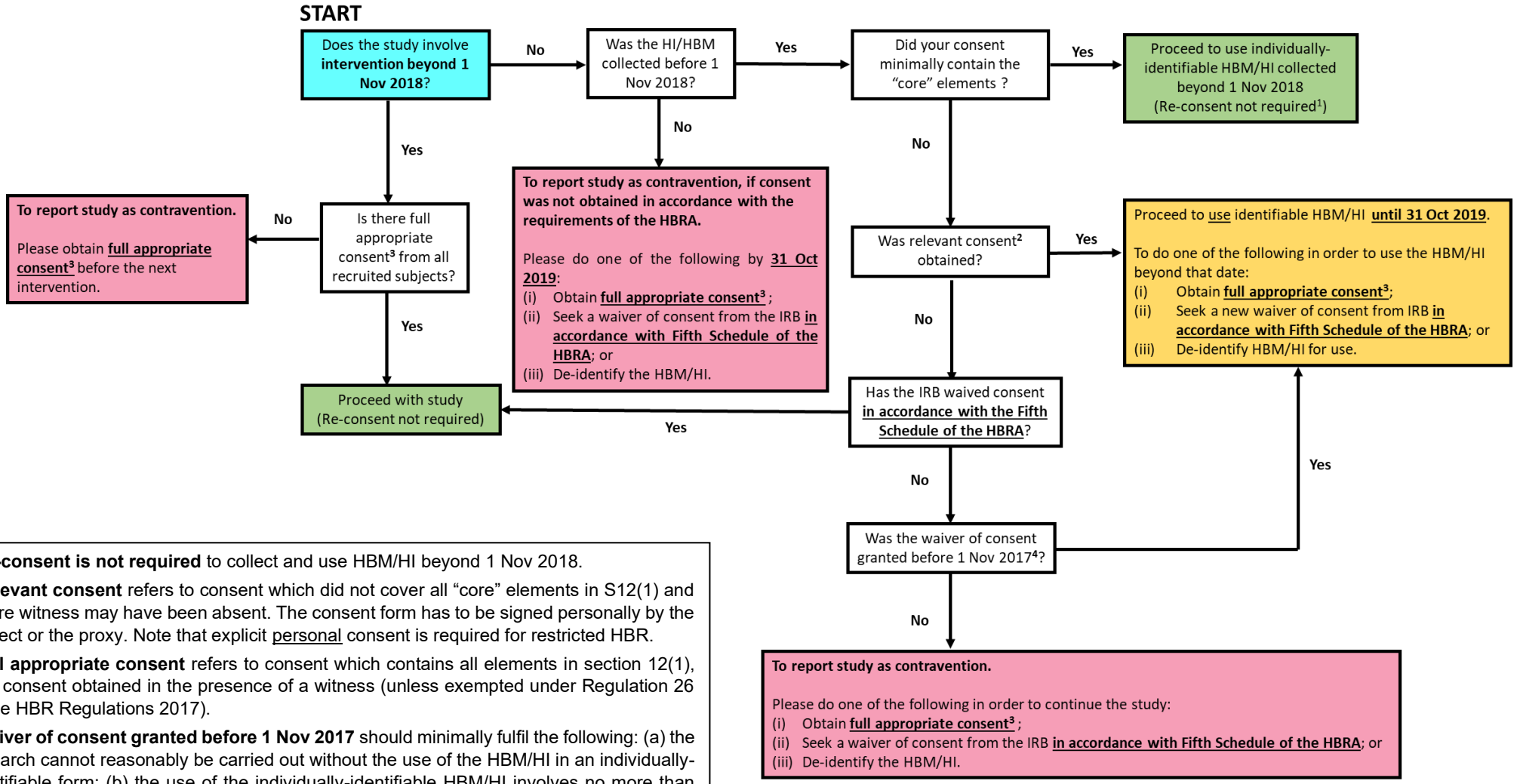
[17] To continue using the HI or HBM in an individually-identifiable form
[18] Witness is not required for consent obtained before 1 November 2017

For a summary of the requirements of consent under the HBRA for ongoing studies, please refer to **Figure 2** below.

❖ **What if re-consent was not obtained by the timeline indicated in this guide?**

For the studies that are required to be reported to HSA as contraventions as outlined above, re-consent will need to be obtained from the research subjects in accordance to the requirements of the HBRA **by the timeline stipulated in the respective sections**. Failure to do so may result in further enforcement actions to be taken by HSA.

Figure 1: Flowchart to determine the appropriate actions required to continue the research beyond 1 November 2019



[1]**Re-consent is not required** to collect and use HBM/HI beyond 1 Nov 2018.

[2]**Relevant consent** refers to consent which did not cover all "core" elements in S12(1) and where witness may have been absent. The consent form has to be signed personally by the subject or the proxy. Note that explicit personal consent is required for restricted HBR.

[3]**Full appropriate consent** refers to consent which contains all elements in section 12(1), with consent obtained in the presence of a witness (unless exempted under Regulation 26 of the HBR Regulations 2017).

[4]**Waiver of consent granted before 1 Nov 2017** should minimally fulfil the following: (a) the research cannot reasonably be carried out without the use of the HBM/HI in an individually-identifiable form; (b) the use of the individually-identifiable HBM/HI involves no more than minimal risk to the research subject; (c) the waiver concerned will not otherwise adversely affect the rights and welfare of the research subject.

Figure 2A: Summary of the requirements of consent for HBR studies involving use of individually-identifiable HI and/or HBM (**without any further intervention**)

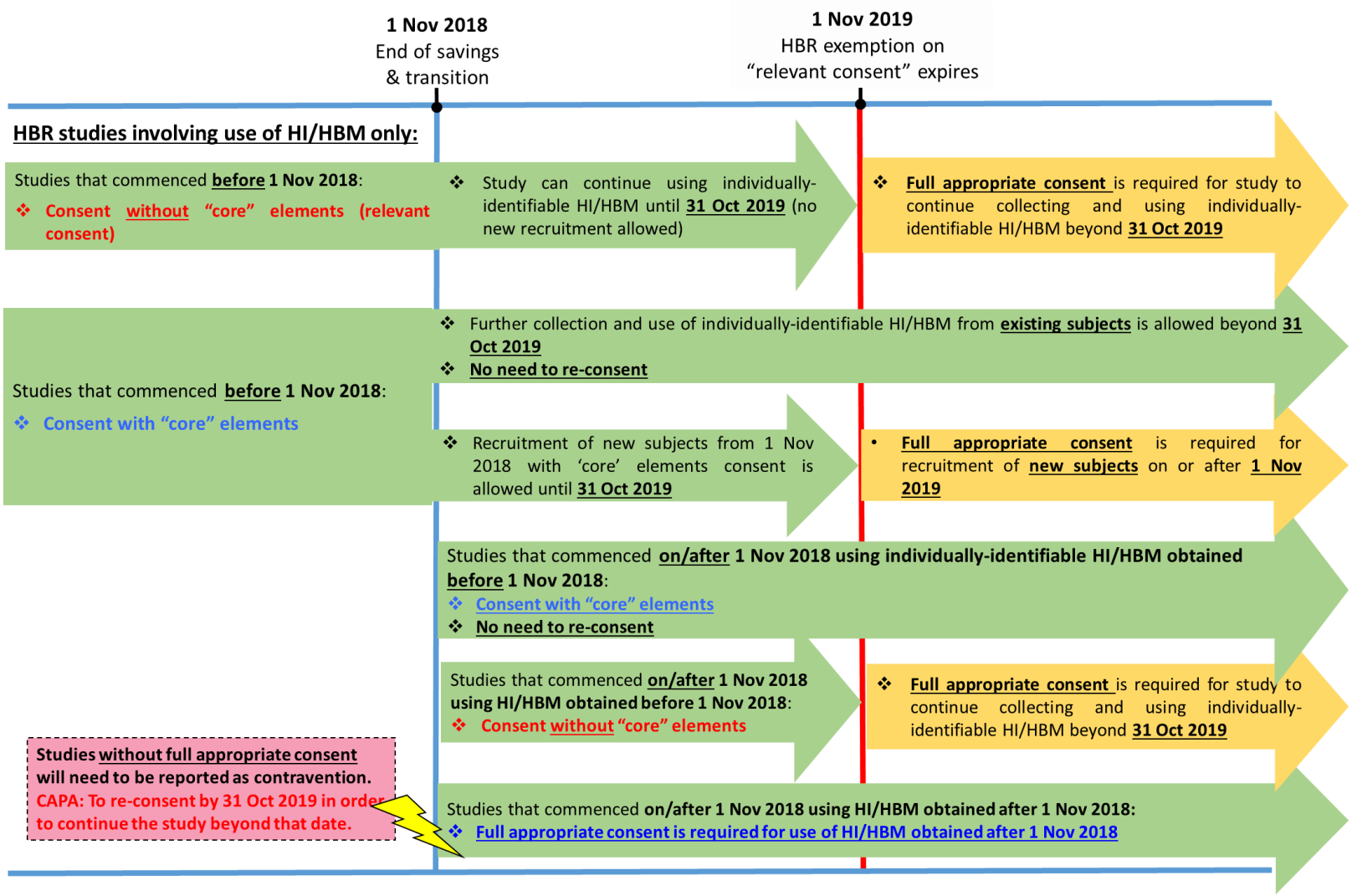
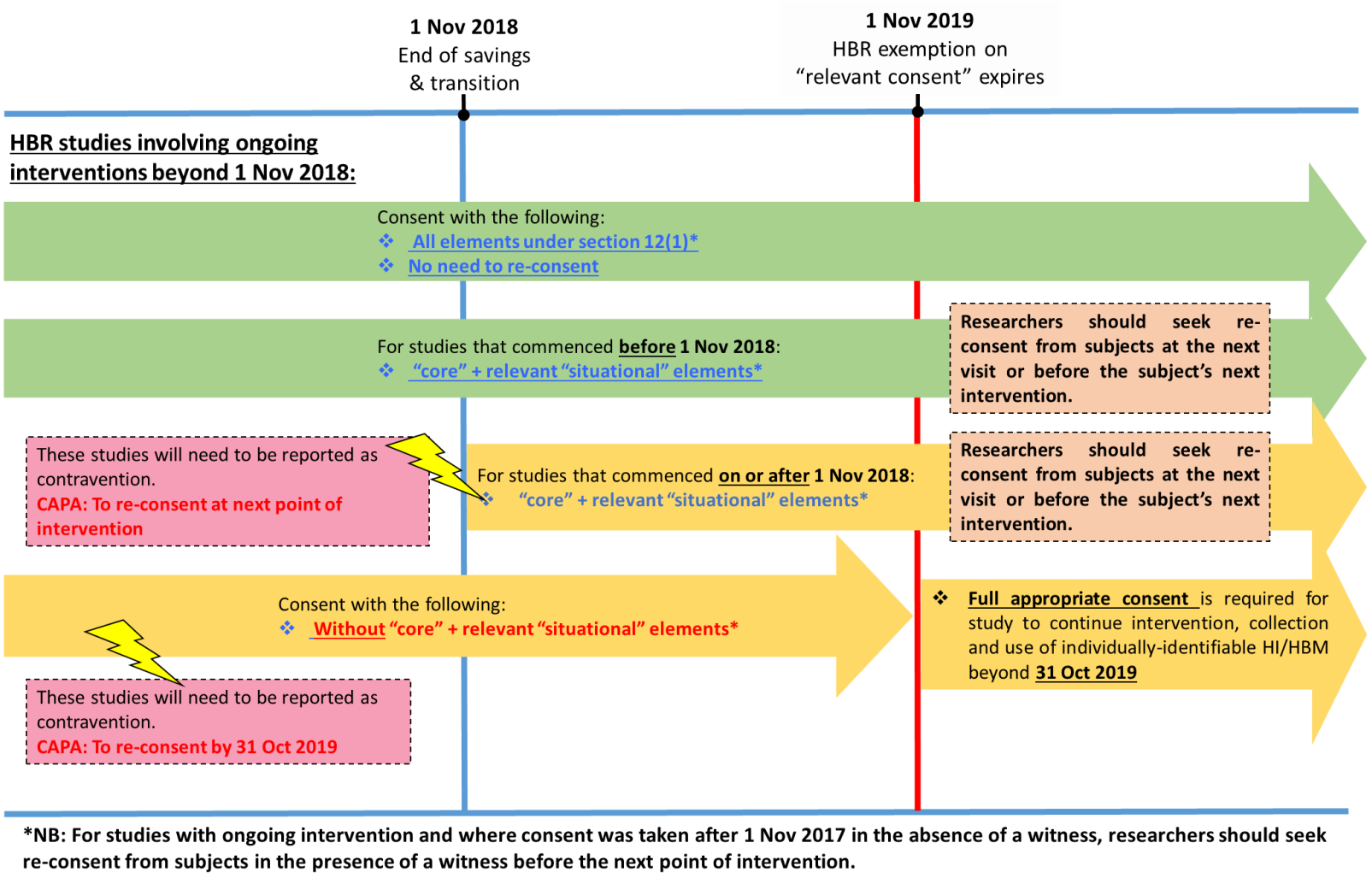


Figure 2B: Summary of the requirements of consent for HBR studies **involving ongoing intervention**[19]



***NB: For studies with ongoing intervention and where consent was taken after 1 Nov 2017 in the absence of a witness, researchers should seek re-consent from subjects in the presence of a witness before the next point of intervention.**

[19] Please see Figure 2A if you have no further interventions in your study.

3. Requirement of consent for handling of human tissue in research

3.1 For handling of human tissue in research where the tissue is collected on or after 1 November 2019

Appropriate consent is required for removal, storage, supply and use of human tissue collected on or after 1 November 2019[20]. Before the consent is obtained, all information elements listed under section 12(2) of the HBRA must be provided. Similarly, even when there is no intention to carry out certain activities covered under section 12(2) (e.g. the donated tissue will not be used in restricted research), the negative fact should still be conveyed to the tissue donor during the taking of appropriate consent (except section 12(2)(k), which is indicated as "where applicable" and can be omitted entirely if it is not applicable to the tissue donation).

Furthermore, where the donation involves **removal of tissue from the donor primarily for research,** the consent must be obtained in the **presence of a witness**, unless the removal procedure is of no more than minimal risk to the donor, the donor is unable to read or sign the consent form, and the tissue will not be used in restricted human biomedical research, in accordance with Regulation 3(2) of the HBR (Requirements for Appropriate Consent – Exemption) Regulations 2019.

3.2 For storage, supply and use of human tissue collected before 1 November 2019

Any tissue collected before 1 November 2019 may only be stored, supplied and used for research with the donor's consent[21]. For such tissue, the **following three mandatory "core" elements of information must be provided** before the donor's consent is obtained:

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

[20] Date in which the regulations of human tissue framework under HBRA will be enacted.
[21] Except for tissue removed from the donor and rendered non-identifiable before the appointed date of section 64 of the HBRA (legacy biological material). Such tissue may be used without donor's consent.

These 3 elements are identified as **"core"**, as these are essential information that should be provided to all tissue donors, in order for them to understand that safety and welfare are being protected when donating their tissue for research purposes.

The remaining 12(2) elements are "situational" elements which should not be carried out if consent was not obtained for these activities. For example, if the consent form did not include the possibility that the donated tissue would be used in human-animal combination research, it will not be permissible for the tissue to be used in such research.

The full list of "core" and "situational" elements in section 12(2) can be found in **Annex A2**.

❖ **When is my tissue considered as 'legacy human biological material'?**

'Legacy human biological material' refers to HBM that had been obtained **and de-identified** prior to the activation date of the Human Tissue Framework (HTF), i.e. 1 November 2019. 'De-identification' may be reversible or **irreversible.**

Where the HI and/or HBM is de-identified such that a re-identification key remains, the organisation should ensure that an 'effective barrier' exists between the key-holder and any person involved in the conduct of tissue banking activities on the legacy HBM, to prevent re-identification of the tissue donor without consent.

❖ **When is re-consenting of tissue donor required?**

Re-consenting of tissue donor with all information elements under section 12(2) is required before 1 November 2019 to store, supply and use the donated tissue in research under the following circumstances:

a. The consent obtained did not provide the three "core" elements of information as stated above in this section; or
b. The tissue is intended to be used for such purposes **beyond the scope of consent obtained or restrictions stipulated by the tissue donor.**

4. Waiver of appropriate consent for the use of individually-identifiable HI or HBM

Where attempting to obtain consent or re-consent would impose such disproportionate burden to the researchers such that carrying out the research is no longer possible, researchers may seek a waiver of appropriate consent from the IRB. To be clear, mere inconvenience, additional costs or time delays resulting from the taking of consent are themselves insufficient to warrant a waiver.

In assessing whether a waiver of appropriate consent should be granted, conditions under the Fifth Schedule of the HBRA must be fulfilled.

❖ **Are researchers allowed to continue their HBR if consent had been waived by an ethics committee before 1 November 2017?**

Researchers are only allowed to continue their existing HBR if the IRB (appointed by the RI supervising the HBR) is satisfied that the conditions stipulated under the Fifth Schedule of the HBRA are fulfilled.

If not, researchers can continue their HBR until **31 October 2019** if the ethics committee which granted the waiver before 1 November 2017 had minimally considered the following:

a) the research cannot reasonably be carried out without the use of the HBM/HI in an individually-identifiable form;
b) the use of the individually-identifiable HBM/HI (as the case may be) involves no more than minimal risk to the research subject; and
c) the waiver concerned will not otherwise adversely affect the rights and welfare of the research subject.

These studies are exempted under the HBR (Exemption) Regulations released on 31 October 2018. For such HBR studies to continue beyond 31 October 2019, researchers should consider one of the following courses of action:

a) **obtain appropriate consent with all elements** listed under section 12(1);
b) **seek a waiver of consent** from the IRB in accordance with the conditions stipulated under the Fifth Schedule of the HBRA; or

c) **use** the HI or HBM in an non-identifiable form research[22].

To better guide researchers in determining the necessary steps that need to be performed to continue their HBR, please refer to the flowchart in **Figure 1**.

4.1 For individually-identifiable HI and/or HBM obtained or compiled before 1 November 2017

The IRB may waive the requirement for appropriate consent if the IRB is satisfied that:

a) the research cannot be reasonably carried out without the use of the HI and/or HBM in an individually-identifiable form;
b) the use of the individually-identifiable HI and/or HBM involves no more than minimal risk to the research subject;
c) the waiver concerned will not otherwise adversely affect the rights and welfare of the research subject; and

***For HI*:**

d) the process of obtaining consent from the person to which the HI relates will involve a disproportionate amount of effort and resources relative to the research requirements;

For HBM:

d) reasonable effort has been made to re-contact the person to which the individually-identifiable HBM relates for the purpose of obtaining his or her consent.

❖ **How should researchers demonstrate that "reasonable effort has been made to re-contact the person"?**

Researchers may consider convenient and practical means of seeking consent from the research subject, such as replying to a letter, email or recording of voice call. Generally, it can be considered that reasonable effort has been made if the research subject remains uncontactable or have not responded after two attempts (reasonably spaced at approximately 30 days apart) have been made to re-contact the subject.

[22] Use of de-identified HI or HBM does not require appropriate consent under the HBR framework

4.2 For individually-identifiable HI and/or HBM obtained or compiled on/ after 1 November 2017

The IRB may waive the requirement for appropriate consent if the IRB is satisfied that:

a) the research cannot be reasonably carried out without the use of the HI and/or HBM in an individually-identifiable form;
b) the process of obtaining consent from the person to which the HBM/HI relates will involve a disproportionate amount of effort and resources relative to the research requirements;
c) the use of the individually-identifiable HI and/or HBM involves no more than minimal risk to the research subject;
d) the waiver concerned will not otherwise adversely affect the rights and welfare of the research subject; **and**
e) the HBR or HI research would reasonably be considered to contribute to the greater public good.

What is the definition of "greater public good"?

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 or regional level with potential direct benefit to the public at large; or
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 a national, regional or international level with potential to lead to improvement in policy and prevailing standards on innovation, management and practice in healthcare and other human biomedical related fields.

Annex A1. Information that needs to be provided for HBR Studies under section 12(1) of the HBRA – 7 Core, 8 Situational Elements

NB: "Core" and "situational" elements in this table only apply in the context of section 2 of this guide, i.e. for HBR conducted during the period 1 November 2018 – 31 October 2019. From 1 November 2019, **ALL** elements (except e and j, if they are not applicable) would need to be provided to research subjects when obtaining consent for their participation in a HBR study.

Elements of 12(1)	Core or Situational	Explanatory Notes
12(1)(a) the **investigational nature** of the biomedical research	Core	These are essential elements as they have significant bearing on the subject's decision whether to participate or not.
12(1)(b) the **purpose** of the biomedical research	Core	
12(1)(c) the reasonably foreseeable **risks**, discomforts or inconveniences to a living research subject arising from this biomedical research	Core	
12(1)(d) the **benefits** which the research subject may reasonably expect from the biomedical research	Core	
12(1)(h) the extent to which information identifying the research subject will be kept **confidential**	Core	Confidentiality is an important element. This has significant bearing on the subject's decision to participate.
12(1)(k) whether the participation of the research subject involves info in **individually-identifiable** form	Core	This element is sensitive and it has significant bearing on the subject's decision.
12(1)(n) the research subject's **right to withdraw** his or her consent in the circumstances specified in section 14 and the limitations of such withdrawal as specified in that section	Core	This is an essential element as it has significant bearing on the subject's welfare and decision whether to participate or not.
12(1)(e) where applicable, whether there are any **alternative procedures or treatments** available to the research subject, and the potential benefits and risks of such alternatives	Situational	For interventional research – where alternative procedures or treatments are available, they should be disclosed to the research subject.
12(1)(f) any **compensation and treatment** available to the research subject **in the event of injury arising** from participation in the research	Situational	Not required if there is no intervention.
12(1)(g) any **anticipated expenses** the research subject is likely to incur as a consequence of participating in the biomedical research	Situational	Not applicable if HBR is solely using HBM/HI already collected and there are no anticipated expenses.

12(1)(i) whether individually-identifiable information obtained from the research subject will be **used for future biomedical research**	Situational	If this was not obtained – Researchers are not able to use the identifiable information for future research.
12(1)(j) where applicable, whether **biological material** taken from the research subject will be **destroyed, discarded or stored for future biomedical research**	Situational	If this was not obtained – Researchers are not able to use the biological material for future research.
12(1)(l) the circumstances, if any, under which, the research subject or the person authorised to give consent under this Part will be **contacted for further consent** e.g. SAE, change in proposed research	Situational	Required if the researcher foresees that there will be circumstances under which the research subject will be contacted for further consent.
12(1)(m) whether the research subject would wish to be **re-identified** in the case of an **incidental finding** if the propose biomedical research expressly provides for such re-identification	Situational	If this was not obtained – Researchers cannot re-identify subjects to return incidental findings if this consent was not obtained.
12(1)(o) the **person or persons to contact** to obtain further information on the biomedical research and to provide feedback in relation to the biomedical research	Situational	This element does not have significant bearing on the subject's decision whether to participate or not. The subject can contact the research institution if there are further queries.

Annex A2. Information that needs to be provided for Tissue Donation under section 12(2) of the HBRA - 3 Core, 14 Situational Elements

NB: "Core" and "situational" elements in this table only apply in the context of section 3.2 of this guide, i.e. for human tissue obtained on or before 1 November 2019. From 1 November 2019, **ALL** elements (except k, if it is not applicable) would need to be provided to tissue donors when obtaining their consent.

Elements of 12(2)	Core or Situational	Explanatory notes
12(2)(a) the **specific research purpose** for which the tissue is intended to be used, if this information is available but if not available, the purpose for which the tissue is intended to be used may be stated as for general research	Core	This is an essential element as it has significant bearing on the donor's decision whether to donate his tissue or not.
12(2)(f) the donor's **right to withdraw** his or her consent in the circumstances specified in section 14 and the limitations of such withdrawal as specified in that section	Core	This is essential in ensuring autonomy of the tissue donor. (Unless it was made clear to the donor that the donation of his tissue is an outright gift and the donation cannot be withdrawn.)
12(2)(i) the extent to which records identifying the donor will be kept **confidential**	Core	Confidentiality is an important consideration. This has significant bearing on the donor's decision to donate his tissue or not.
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	Situational	If this was not obtained – The tissue cannot be used for any purpose other than research.
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)	Situational	This is only required where the IRB had waived the requirement that the removal of the tissue is primarily for a therapeutic or diagnostic purpose – i.e. for 1. Mentally incapacitated adults/minors; or 2. Minors who lack sufficient understanding and intelligence to give consent.
12(2)(d) the reasonably foreseeable **risks**, discomforts or inconveniences to a living donor arising from the **removal of the tissue**	Situational	Only required if the donation involves tissue removal.

12(2)(e) the donation of the tissue is voluntary and the **renunciation of the donor's rights to the tissue and any intellectual property rights** that may be derived from the use of the tissue	Situational	If this was not obtained – It cannot be taken that the donor has renounced his rights to the tissue and any intellectual property (IP) rights that have been derived from the use of the tissue.
12(2)(g) any **compensation** and treatment available to the donor in the event of injury arising from participation in the process of tissue donation	Situational	Not required if there is no intervention (i.e. tissue has already been collected).
12(2)(h) any **anticipated expenses** the donor is likely to incur as a consequence of donating tissue	Situational	Not required for tissue that has already been collected and there are no anticipated expenses.
12(2)(j) whether individually-identifiable **information** obtained from the tissue donor will be **used for future research**	Situational	If this was not obtained – Researchers are not able to use the identifiable information for future research.
12(2)(k) where applicable, whether **biological material** taken from the tissue donor will be **destroyed, discarded or stored and used for future research**	Situational	If this was not obtained **–** Researchers are not able to use the biological material for future research.
12(2)(l) whether, and the circumstances under which, the donor or the person authorised to give consent under this Part, as the case may be, will be **contacted for further consent**	Situational	Required if the researcher foresees that there will be circumstances under which the tissue donor will be contacted for further consent.
12(2)(m) whether the tissue donation would result in the use of the donor's tissue in an **individually-identifiable** form	Situational	If this was not obtained – Tissue cannot be supplied for use in an identifiable form.
12(2)(n) whether the tissue will be used in **restricted human biomedical research** involving human-animal combinations	Situational	If this was not obtained – Tissue cannot be used in restricted research.
12(2)(o) whether the donor or the person authorised to give consent under this Part, as the case may be, would wish to be **re-identified in the case of an incidental finding** if the future research expressly provides for such re-identification	Situational	If this was not obtained – Researchers cannot re-identify tissue donors to return incidental findings if this consent was not obtained.
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	Situational	This element does not have significant bearing on the donor's decision whether to participate or not. The donor can contact the research institution if there are further queries.
12(2)(q) whether the tissue will be **exported or removed** from Singapore to a place outside Singapore	Situational	If this was not obtained – The tissue cannot be exported to a place outside Singapore.

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