SOP Title: Quarantine, registration and audit of collections

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CHANGE HISTORY

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2. PURPOSE AND SCOPE

2.1 The University must provide assurance that all human tissue stored, on all premises relevant to the scope of the Human Tissue Authority (HTA) licence 12217, is identified, catalogued and within the governance arrangements for licence 12217.

NOTE: 1 For further information on the Human Tissue Act, HTA Codes and Standards, HTA licence 12217 and individual responsibilities see HTA011.

2.2 The purpose of this SOP is:

a) To define the procedure for accepting sample collections under licence 12217 under quarantine measures while governance checks and audits are carried out to ensure that full registration of a new collection will not unduly increase the risk of non-compliance on licenced premises.

b) To define the procedure for registration and audit of sample collections stored under the governance of HTA licence 12217.

c) To define the procedure for conducting follow-up compliance audits of sample collections stored under the governance of licence 12217. The HTA expects the Designated Individual (DI), or nominated representative, to make regular visits to any and all satellite premises to verify that the governance systems are working. This SOP provides a formal mechanism for carrying out these visits.

d) To ensure audits lead to timely preventative and corrective actions when necessary and to monitor and enhance the level of compliance across all collections registered.

2.3 This SOP applies to all personnel working under HTA licence 12217 who collect, use or store relevant material tissue for scheduled purposes.

2.4 Exclusions:

a) This does not apply to sample collections that are already under the governance of other University licences (12168 Clinical Trials Service Unit, 12326 Oxford Centre for Diabetes Endocrinology & Metabolism, 12433 Weatherall Institute of Molecular Medicine, 22496 Oxford DRWF Human Islet Isolation Facility, or 12178 Medical Sciences Teaching Centre).

b) This does not apply to sample collections held under a current and valid approval from a recognised research ethics committee (REC). Note: University ethics committees are not considered to be a recognised REC.
3. PROCEDURE FOR REGISTRATION

3.1 Quarantine of existing collections prior to registration

NOTE 2: This Section of the SOP is intended to enable the DI and Licence holder to meet specific Directions imposed on the HTA licence by the Human Tissue Authority from 24th July 2017 (See 6.1, Appendix 1).

NOTE 3: According to the specific Directions imposed on HTA licence 12217, any newly discovered existing collections on licenced sites must be notified to the HTA within 5 working days. The notification is the responsibility of the DI and the Corporate Licence Holder.

NOTE 4: Existing sample collections may only be stored in quarantine for a limited period agreed at the time of registration, to enable one of the following actions; disposal, transfer elsewhere, cover by a new application for ethics approval from a recognised REC or registration under the full governance of the HTA licence.

3.1.1 Procedure for investigators / sample custodians

a) Any existing collections of relevant material on sites licenced by 12217 must be immediately brought to the attention of the Human Tissue Governance Team (HTGT) by completing and returning a Registration form\textsuperscript{9}.

b) The relevant Person Designated (PD) must be made aware of all collections under their remit.

c) If required, complete any procedure to report adverse events or non-conformities as detailed in licence core SOP HTA003\textsuperscript{8}.

d) The samples must be held in quarantine until an audit of the collection against the HTA’s Standards for Research\textsuperscript{11} can be adequately completed to allow them to be lawfully registered and stored under the governance of the HTA licence.

e) The quarantine imposed is both a physical and communicated quarantine:

i. Quarantined samples must be clearly labelled to indicate that they have been put under quarantine for HTA licence 12217.

ii. No samples must be removed or added to the collection without the express permission of the DI. Permission will only be given for exceptions, for example, to enable consent withdrawal requests to be fulfilled.

iii. The quarantine must be communicated to all persons with access to the storage area and involved with the collection, processing, use, storage or disposal of the samples to ensure that no samples are inadvertently removed or added.
f) Prepare evidence of compliance with the HTA’s Standards for the Research sector for audit, as directed by the HTGT.

g) Schedule a compliance audit with the HTGT and address any shortfalls identified during the audit.

h) Once the collection has been demonstrated to be stored according to the HTA Standards, the collection can be stored under the governance of the licence, and the quarantine can be removed. Follow the procedure in section 3.2.1 g) (Registration of a sample collection under licence 12217, Procedure for investigators / sample custodians).

3.1.2 Procedure for Persons Designated (PD)

a) Provide guidance to personnel within each PD’s remit regarding the procedures to follow to transfer an existing collection under the governance of the licence.

b) Assist the sample custodian throughout the registration process and escalate any problems arising to the HTGT and DI, who may seek support from the relevant Head of Department if needed, in order to remove any obstacles to compliance.

c) Ensure the DI’s instructions are acted upon with regards to the quarantine procedure and/or any instruction to dispose of samples.

3.1.3 Procedure for the Human Tissue Governance Team (HTGT)

a) Upon receipt of a completed Registration form, the HTGT will check that the collection has not already been registered then details of the collection must be added to the Human Tissues Licenced Collections Database (HuLC).

b) Upon receipt of a completed Registration form, the HTA must be notified within 5 working days of any newly discovered existing collection. Associated with this, the HTA must be notified:

   i. If it is the intention to dispose of the collection;

   ii. If there has been any breach of the licensing or consent requirements of the Human Tissue Act 2004.

c) Newly discovered existing collections must be triaged by the HTGT to determine if the HTA notification needs to include any information on breaches or disposal, as detailed in core SOP HTA003 – Incident Reporting. Log and investigate any adverse events associated with the collection.

d) For samples collected on or after 1st September 2006 evidence must be collected of written records of consent or an appropriate agreement covering the samples if transferred from a third party. This is described in the Core HTA licence SOP for Consent (HTA001). The consent form and participant information must allow for on-going storage of the samples.

e) Reasons that consent may not be adequate include:

   i. Consent was not recorded

   ii. The person seeking consent was not trained
iii. The consent was restricted to keeping the samples for a limited time period now expired

iv. The consent is restricted in ways meaning that the samples can’t be safely stored under the governance of the licence (e.g. they could only be used for research relating to the specific aims and objectives of the study for which they were collected)

f) Evidence must be collected that samples are catalogued. If there is not a sample inventory or register in place at the time of discovery, arrangements must be made to have a fully audited, clean and accurate inventory in place within agreed timelines.

g) Evidence must be collected that donors are not identifiable by the researcher(s) accessing the samples. Arrangements must be made for samples labelled with names, other personal identifiers or initials if they are from staff / student healthy volunteers (because initials would be enough to enable identification of the persons from which the samples came) to be re-potted, over-labelled or disposed of.

h) Schedule and carry out an audit of the collection against the HTA Standards for Research, as detailed in Section 4. Any shortfalls against the standards must be addressed before the samples can be fully registered under the governance of the HTA licence and the quarantine removed.

i) Ensure the DI retains oversight throughout the process.

3.2 Registration of a sample collection under licence 12217

NOTE 5: For a sample collection to be stored under licence 12217 it must meet all the requirements of the HTA Code and Standard for Research.

NOTE 6: The basis of an application to store samples under licence 12217 is a Registration form[6] which must be completed and submitted to the HTGT with accompanying documentation. The information provided determines if the sample collection meets the requirements of the HTA Standards for Research. This Registration form is used to notify HTGT of existing collections and new sample collections.

NOTE 7: This section is to be followed to register new sample collections that are transferring from other institutions and/or an appropriate existing ethics approval. For existing sample collections the procedure described in section 3.1 - Quarantine of existing collections prior to registration, must be followed.

NOTE 8: Registration is necessary to prevent a breach of the Human Tissue Act. For a new collection, if proof of compliance with the HTA Code and Standard for Research is not available for auditing, the procedure described in section 3.1 Quarantine of existing collections prior to registration, must be followed.

3.2.1 Procedure for investigators / sample custodians
a) Contact the relevant PD to make them aware of the new collection to be registered.

b) Work with the PD to collate and collect the information necessary to the registration process, for example details of custodial responsibility, ethical approval(s), number of samples.

c) Allow sufficient time to complete the registration before the samples are transferred from another institution or licence, and/or before any exemptions to licensing such as ethics approval are allowed to lapse. This is to avoid breaching the licensing requirements of the HT Act.

d) Complete a Registration form. A completed copy of the Registration form must be submitted to the HTGT.

e) Provide the relevant documentation to evidence that the HTA Standards for Research are met. This may require standard operating procedures (SOPs) to be drafted, reviewed and approved and risk assessments may need to be carried out if not already in place. Template SOPs and RAs are available from the HTGT.

f) Schedule a compliance audit with the HTGT and address any shortfalls identified during the audit. Complete incident reporting procedures if necessary.

g) Display a copy of the HTA licence in all storage areas containing samples registered under licence 12217.

h) Prepare and agree with the PD a schedule of internal audits for the collection (see core SOP HTA004 on Quality). Perform the required internal audits following the schedule.

i) Comply with regular audits by the PD following a 12-month schedule.

j) Provide annual updates to the HTGT on the sample collection. Submitting these updates is a requirement of storing samples under licence 12217. These updates include:

   i. Any changes to the governance arrangements of the collection (e.g., change of PI);

   ii. Any changes to the storage arrangements and/or location(s) of the samples;

   iii. Details of sample accruals and up-to-date total number of samples of relevant material in the collection;

   iv. Details of any samples released to researchers;

3.2.2 Procedure for Persons Designated
a) Identify the person who will be responsible for the collection (this may be the Principal Investigator of the study under which the samples were collected or another investigator who has inherited the collection and agreed responsibility). This person is ultimately responsible for registering the collection under the HTA licence, even though they may choose to use a nominated representative.

b) Identify the institution that has custodial responsibility. If custodial responsibility lies with an institution other than the University of Oxford, it may be appropriate to arrange to transfer the sample collection to the custodian in Oxford. In this case, involve the HTGT who will discuss how to proceed with the team at Clinical Trials and Research Governance (CTRG).

c) Ensure that all people involved with the collection, processing, storage, use and disposal of the sample collection have:

i. Completed a Human Tissues Training Declaration and have completed the University HTA training on WebLearn®. The training must be completed and the assessment passed by everyone working with the samples under the governance of licence 12217 before the sample collection can be fully registered.

ii. Are aware of where to find copies of the Licence Policy®, Registration Guidance®, Licence Core SOPs and Risks Assessments as well as templates for SOPs and Risk Assessments.

d) Assist the HTGT to ensure areas of non-compliance are flagged, corrected and escalated if necessary.

3.2.3 Procedure for HTGT

a) Upon receipt of the registration form, details of the collection must be added to the Human Tissues Licenced Collections Database (HuLC).

b) Assist the investigator / sample custodian and Person Designated through the registration process. If necessary, review documentation and identify any gaps in documentation.

c) Work with CTRG and the DI to solve any issues regarding the custodianship of material and checking the validity of any ethics approval if required.

d) In order to finalise registration and to assess the level of compliance with the HT Act, the terms of the licence, and University policies and procedures, carry out an audit of the sample collection, premises and documentation using the Audit Form against the HTA Standards for Research®.

i. Any area of non-compliance must be highlighted for rectification; responsibilities and timescales must be agreed between the sample custodian and HTGT for corrective actions. A summary of non-compliances / non-conformities, together with agreed corrective actions must be documented and provided to the custodian / PI using the Audit Summary Form®.

ii. Any collection found to be stored in breach of the HT Act must be put into quarantine (see relevant parts of section 3.1) until the audit has been
completed to determine the correct course of action, and the procedure for incident reporting followed.

e) Forward copies of the Audit Summary form to the relevant PD so that they may assist the sample custodian / PI in addressing shortfalls.

f) Provide the sample custodian with a copy of the HTA licence to display in all storage areas.

g) Add the collection to the HTGT audit schedule and arrange for the collection to be added to the PD's peer-to-peer audit schedules.

h) Log any changes to the collection as documented in the annual returns into the HuLC database.

4. PROCEDURE FOR AUDITS

NOTE 9: The purpose of the audits detailed in this SOP is to document how the governance and/or procedures supporting a sample collection meet the HTA Standards for Research, or to monitor compliance with licence core procedures.

NOTE 10: The audit should be a two way communication process; gathering relevant information and providing support to remind and inform people working under the licence of requirements and responsibilities.

4.1 Running an Audit

4.1.1 Procedure for HTGT:

a) The initial registration audit (to be conducted for quarantined collections as well as for new collections) must cover all aspects of the HTA Standards for Research including:

   i. Consent;

   ii. Governance and quality systems (e.g. governance meetings, documentation in place, document control, contracts and agreements, non-conformities and corrective and preventative actions, staff training and competency, risk assessments, record keeping);

   iii. Traceability including disposal;

   iv. Premises, Facilities and Equipment (including security and confidentiality, cleaning and decontamination, monitoring of storage conditions, contingency provisions, equipment maintenance and calibration, personal protection equipment).
b) To conduct the audit use the Audit Form HTA against the Standards for Research as a guide and to record the details of evidence of meeting the standards. Use the form to note concerns if standards are not met.

c) To formalise the audit, use the Audit Summary Form to complete a written report of the audit, detailing all audit findings, providing a copy to the person responsible for the collection, or their nominated representative.

d) A bi-directional traceability audit must be carried out as part of the audit for registering quarantined collections and new collections (see section 4.1.2 f) below).

e) Other audits may be conducted by the DI and/or the HTGT against HTA standards and/or licence processes and procedures.

f) The DI and/or the HTGT will make a risk based and proportionate decision on when and how often to visit a site. This may depend on a number of factors including:

   i. The audit schedule provided by a PD for a particular site

   ii. The outcomes of local audits by the PD

   iii. The outcome of inspection by the HTA

   iv. Any adverse events/ incidents that are reported relating to a particular collection, responsible person, PD and PI

   v. Attendance at the Governance meetings

   vi. Other information that is provided about the premises and/or the collection and the work of the HTA Licence Risk Management Committee (see the Licence 12217 Constitution for details of this committee).

g) Reasonable notice will be given to the person responsible for the collection, or their nominated representative, and the PD of the site of the intention to visit the premises and carry out an audit.

   i. At the initial request to visit, advice will be provided on the format that the audit will take and on the kinds of documents that should be made available to facilitate the audit process and to ensure the appropriate people are available and present at the audit.

   ii. Template copies of the audit SOP and forms will be provided in advance (this SOP for Registration and Audit, Traceability Audit Form, Audit Form against HTA Research standards).

h) The HTGT should review previous registration documentation and records relating to the collection and the premises, including the findings of previous audits and any adverse events, to help guide the focus of the audit.

i) As part of an audit, the DI and HTGT may:

   i. Investigate a specific concern
ii. Select at random two specific HTA standards

iii. Check that the people working under the licence know where to find SOPs, policies, logs and guidance provided centrally by the HTGT and that current versions have been acknowledged and are being used

iv. Check that people working under the licence have received documented training.

4.1.2 Procedure for Persons Designated

a) For collections fully registered under the licence, ensure a 12-month cycle audit schedule is in place for each site. The audit schedule may include vertical audits which may focus on a specific sample collection or horizontal audits which may focus on a particular aspect of the HTA Standards for Research.

b) The audit cycle as a whole must cover all aspects of the HTA Standards\(^5\). For each collection, pick at random one main area of the standards to investigate, from the following:

i. Consent

ii. Traceability

iii. Governance and Quality Management

iv. Premises, Facilities and Equipment

c) To conduct the audit use the relevant sections of the Audit Form HTA against the Standards for Research\(^9\) as a guide and to record the details of evidence of meeting the chosen standards. Use the form to note concerns if standards are not met.

d) To formalise the audit, use the Audit Summary Form\(^10\) to complete a written report of the audit, detailing all audit findings, providing a copy to the person responsible for the collection, or their nominated representative.

e) Each audit must also include a bi-directional audit as described below.

f) Example Audit: Traceability Audit

NOTE 11: For traceability, a bi-directional audit provides an indication of the robustness of the systems that are in place to track and trace samples.

i. To carry out a bi-directional audit, complete the Traceability Audit Form\(^11\).

ii. Select 2 sample records at random from the inventory system / sample register and trace the records to:

   a. the consent form (if applicable, see NOTE 12 below)

   b. the physical location of the samples

iii. Select 2 samples at random from the physical storage location and trace the records to:

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a. the consent form (if applicable*)

b. the inventory system.

NOTE 12: The consent form is not required for audit if the samples were collected before 1st September 2006, the specimens have been imported or consent was gained by a third party and a copy of the agreement (e.g. SLA, MTA, Collaboration Agreement) is available to confirm appropriate consent is in place. If one of these exceptions applies, note it in the Comments section of the Traceability Audit Form.

4.2 Audit findings and actions

4.2.1 Procedure for Persons Designated, DI and HTGT

a) The findings of the audit should be discussed with the person responsible for the collection, or their nominated representative, at a close-out audit meeting held within one week of the audit.

b) The person responsible for the collection, or their nominated representative, must be provided with copies of all audit documentation.

i. The PDs must keep records of audits completed against the audit schedule for their site

ii. The HTGT must keep records of registration audits, audits completed by PDs against the audit schedule for their site, any further audits run by the DI and HTGT and audits run by external bodies (e.g. HTA)

c) If an audit raises concerns, e.g. about a lack of robustness of the specimen inventory or if consent records are found to be substandard, this needs to be documented. The Audit summary form will outline required actions, persons responsible and deadlines so that the person responsible for the collection, or their nominated representative, can make arrangements for corrective actions to be carried out.

d) Significant non-conformities, including breach of the HT Act 2004, must be referred immediately to the HTGT after completion of the audit to limit the delay in implementing corrective actions. The procedure for reporting incidents / adverse events is detailed in the Core HTA licence SOP for Incident Reporting. This form must be completed by the person responsible for the collection, or their nominated representative, and returned to the HTGT.

e) Major non-conformities include:

i. Failure to provide evidence of consent where applicable

ii. Failure to confirm traceability of samples

iii. Failure to demonstrate adequate documentation and/or document control

iv. Failure to demonstrate adequate staff training

v. Failure to demonstrate adequate monitoring and preventative measures for secure sample storage
f) Minor non-conformities may be corrected during the audit which records that this has been done. Minor non-conformities include

   i. raising a minor change request to a document

   ii. updating a training record if evidence is provided that training has been completed

h) Any collections found to be stored in breach of the HT Act 2004 are put into quarantine (see section 3.1) until the audit and/or nonconformity has been completed to determine the correct course of action.

NOTE 13: Appropriate timelines for remedial actions to be completed must be specified, risk based and proportionate. Moreover, it may be necessary to raise additional corrective actions than initially described in the root cause document.

NOTE 14: If timelines to complete corrective actions are not met and no reasonable explanation is given, the DI will seek the help of the relevant Head of Department.

NOTE 15: Additional follow-up/audit may be required to confirm ongoing compliance.
5. INTERNAL AND EXTERNAL REFERENCES

5.1 Internal References

11 HTGT guidance on the Human Tissue Act, HTA Codes and Standards, HTA licence 12217 and individual responsibilities (HTA011)
12 Licence 12217 Registration form (HTA_FRM001)
13 HTGT core SOP on Incident Reporting (HTA003)
14 HTGT core SOP on Consent (HTA001)
15 HTGT core SOP of Quality Management (HTA004)
16 HTGT training on the HT Act, HTA standards and licensing requirements (WebLearn): https://weblearn.ox.ac.uk/portal/site/medsci.hla/tool/6d7994d2-a109-4536-8e36-856e6f6c1170
17 Licence 12217 policy on human tissues (HTA007)
18 Registration guidance for licence 12217 (HTA010)
19 Audit Form against HTA Standards for Research (HTA_FRM002)
20 Audit summary form (HTA_FRM005)
21 Traceability audit form (HTA_FRM004)
22 Licence 12217 Constitution (HTA008)
23 Adverse event form (HTA_FRM003)

5.2 External References

6. APPENDIX

6.1 Directions issued by the HTA for licence 12217

The Licence Holder and the DI for licence 12217 have been issued with legal Directions which came into force on 24th July 2017. These Directions mandate that:

a) The DI and licence holder will ensure that all human tissue stored on all premises relevant to the scope of 12217 for a scheduled purpose is identified, fully catalogued and brought within the governance arrangements of 12217. The timeframe for achieving this will be agreed in the CAPA plan.

b) The DI and licence holder will ensure that all governance arrangements and practices under licence 12217 are reviewed and strengthened in line with the CAPA plan.

c) The DI and licence holder will notify the HTA of the following within 5 working days of discovery:

i. Any breach of the licencing or consent requirements of the HT Act 2004

ii. Any newly identified collection to be added to the licence

iii. Any collections to be disposed of.