## SOP Title

### Quality Management

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## CHANGE HISTORY

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<tr>
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</tr>
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<tbody>
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<td>N/A</td>
</tr>
</tbody>
</table>
## 1. TABLE OF CONTENTS

CHANGE HISTORY .............................................................................................................. 1
1. TABLE OF CONTENTS .............................................................................................. 2
2. PURPOSE AND SCOPE ............................................................................................ 3
3. PROCEDURE TO ENSURE COMPLIANCE WITH THE HTA STANDARDS FOR QUALITY MANAGEMENT AND GOVERNANCE ........................................... 4
  3.1 Governance arrangements ...................................................................................... 4
  3.2 Documentation ........................................................................................................ 4
  3.3 Audits ..................................................................................................................... 6
  3.4 Staff training .......................................................................................................... 8
  3.5 Risk management ................................................................................................. 9
  3.6 Adverse events ..................................................................................................... 10
  3.7 Management of records ...................................................................................... 10
4. INTERNAL AND EXTERNAL REFERENCES ................................................................. 11
  4.1 Internal References ............................................................................................... 11
  4.2 External References .............................................................................................. 11
5. APPENDICES ............................................................................................................. 12
  5.1 Overview of licence documentation .................................................................... 12
  5.2 Process for problem solving following local audits ............................................. 13
2. PURPOSE AND SCOPE

2.1 The Human Tissue Act 2004\textsuperscript{E1} (HT Act) was implemented on 1\textsuperscript{st} September 2006 to ensure the safe and ethical collection, use and storage of human tissue (relevant material\textsuperscript{E2}). This is regulated by the Human Tissue Authority (HTA), which is an independent non departmental public body of the Department of Health.

2.2 In order to meet the HTA’s licensing standards for Governance and Quality Systems\textsuperscript{E3}, the University must demonstrate that a suitable governance framework is in place, underpinned by clear and controlled documentation, effective audit, staff training and organised record-keeping.

2.3 This Standard Operating Procedure (SOP) defines the requirements for quality management for all collections registered under HTA licence 12217. This SOP sets out how the University will ensure that:

a) All aspects of the work conducted under the licence are governed by documented policies and procedures as part of the overall governance process.

b) There is a documented system of audit.

c) Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.

d) There is a systematic and planned approach to the management of records.

e) There are systems to ensure that all adverse events are investigated promptly.

f) Risk assessments of the establishment’s practices and processes are completed regularly, recorded and monitored.

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

2.5 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.

2.6 Conforming to the directions contained in this SOP is a requirement for registration of collections under the licence and carrying out licensed activities.

2.7 For sample collections stored under the governance of licence 12217, local SOPs detailing procedures on quality management must comply with the procedures in this core SOP.
3. PROCEDURE TO ENSURE COMPLIANCE WITH THE HTA STANDARDS FOR QUALITY MANAGEMENT AND GOVERNANCE

3.1 Governance arrangements

**NOTE 1:** Details of the governance arrangements for licence 12217 are documented in the Licence Constitution\(^{11}\) which gives a high level overview of the committee structures, remit, terms of reference and lines of accountability.

3.1.1 Any local governance arrangements in place for collections registered under the licence (e.g. for Departments, Institutes, individual buildings or Research Tissue Banks) must be documented, with details of any committees and their terms of reference, roles and responsibilities as well as reporting lines and accountability.

3.1.2 Minutes of any formal meetings relevant to licensed activities must be kept, with details of action points and follow-up on the completion of these. The minutes should be disseminated to all relevant staff to ensure personnel working under the licence are aware of all important information relating to the licensed activities they undertake.

3.1.3 National and local information relevant to licensed activities (e.g. communications from the HTA, change in licence level policies) should be disseminated to relevant staff by Departmental Persons Designated (PDs) who will be instructed to do so by the Designated Individual (DI) and the Human Tissue Governance Team (HTGT) on behalf of the DI.

3.1.4 There must be documented complaints management systems; if overarching systems are used (e.g. the Oxford University Hospitals NHS Foundation Trust (OUH) procedure), staff must be aware of how to respond to complaints. Refer to CTRG core SOP 009 for the University procedure for managing complaints arising from clinical research\(^{12}\).

3.2 Documentation

**NOTE 2:** The documentation for the licence is organised into levels, with the highest level being the Licence Constitution\(^{11}\) and an overarching Policy on the use and storage of human material for research\(^{13}\). The Core SOPs, Risk Assessments (RAs) and an overarching Quality Manual\(^{14}\) constitute the second level. The third level is made up of the documents that are required at local level for sample collections held under the governance of the licence and includes local SOPs that are compliant with the core SOPs and local risk assessments. This is shown schematically in 5.1.

3.2.1 SOPs are required to ensure that licensed activities are undertaken consistently, in accordance with regulatory requirements. A list of SOPs that are required at local level for sample collections stored under the licence is given below. Generic template SOPs are provided by the HTGT for local adaptation in order that licensed activities are undertaken consistently. If SOPs are already in place and are consistent with the procedures in the Core SOPs, these do not need to be re-written.

a) Production and control of SOPs

b) Informed consent, including withdrawal of consent

c) Induction and training
d) Internal audit  
e) Security and storage  
f) Equipment use and maintenance  
g) Sample collection  
h) Sample receipt and logging  
i) Sample labelling, sample tracking and sample use  
j) Specimen preparation / preservation  
k) Transporting Samples  
l) Cleaning and decontamination  
m) Laboratory contingency plan  
n) Data contingency plan  
o) Human material disposal (if more detail is required than in the Core Disposal SOP HTA005)  
p) Management of records  

3.2.2 A documented process should detail creation, review, amendment, release and recall of key documents. The process should include mechanisms for ensuring that staff know how to access the current version of a document.  

3.2.3 Local SOPs must be consistent with the instructions contained in core SOPs. In addition to this SOP on Quality Management, the core SOPs for the licence cover Consent, Traceability, Incident Reporting, Disposal, and Quarantine, Registration and Audit.  

3.2.4 A system for document control must be in place for key local documents; SOPs must feature document control information. At a minimum this should include:  
a) Version number  
b) Approval status (i.e. draft, in review, authorised)  
c) Date the document is effective from  
d) Page numbers  
e) Change history  
f) The name of author, reviewer and approver  
g) The date of next review.  

3.2.5 University core SOPs\(^2\) 001 (Generation and control of SOPs) and 014 (Version control) detail the procedures to follow for implementing document control.  

3.2.6 Only current, approved, non-editable versions of SOPs must be available at the point of use. Non-authorised modifications to SOPs are not permitted.  

3.2.7 Documents must be reviewed regularly. At a minimum, SOPs must undergo review at least every three years. Any controlled copies of the obsolete document must be
recalled and destroyed and new controlled copies issued, if applicable. One copy of superseded versions, retired or withdrawn documents must be archived and other copies disposed of appropriately.

NOTE 3: For core HTA SOPs, the copies available on the Research Services website and the WebLearn platform are the only controlled copies; any copies printed or saved elsewhere are uncontrolled copies.

3.2.8 As well as the scheduled review, SOPs may be amended / updated in the event of an adverse event / incident as part of the corrective and preventative actions (CAPA) resulting from the incident. Furthermore, SOPs may be reviewed and amended if a change in procedure is identified as a CAPA resulting from audit findings.

3.2.9 Personnel working under the licence may request amendments to core SOPs by emailing the HTGT to raise an amendment request; amendments will be made at the discretion of the HTGT and DI.

3.2.10 Upon release of a new SOP or a new version of a SOP, all relevant staff must acknowledge that they have read and understand the new document or version.

3.2.11 For core SOPs this is achieved through electronic acknowledgement of new documents and versions in the WebLearn platform. Acknowledging a document in WebLearn using your University of Oxford Single Sign On is the equivalent of an electronic signature and is binding.

3.2.12 Local procedures must be in place to ensure records are kept showing staff acknowledgement of new or amended SOPs.

3.2.13 Other key documents such as forms (e.g. consent forms, tissue request forms, audit forms etc.) and risk assessments must be document controlled as above.

3.3 Audits

NOTE 4: An audit is the inspection or examination of a process or system, to ensure compliance to agreed standards. In this context, the purpose of audit is to measure the sample collections strengths and weaknesses against its own SOPs, the Core SOPs and against the HTA standards.

3.3.1 Principal Investigators / sample custodians must ensure that procedures in the collection(s) they are responsible for comply with:
   a) Legislation and regulations, including the HT Act
   b) Licence 12217 procedures
   c) University policies
   d) Local procedures as documented in local SOPs.

3.3.2 This is achieved through the implementation of a documented schedule of internal audits. It is the responsibility of the collection custodians to ensure that schedules of audit are drawn up for their collections and to make sure the schedule is followed after approval by the relevant PD. This is monitored by the HTGT who will audit collections
to check adherence to audit schedules. If audits are not performed or are performed late, reasons for this must be documented.

**NOTE 5:** In addition to internal audits, a full audit against the HTA standards for the research sector is conducted by the HTGT upon registration of a collection under the licence. Further audits against some of the standards are conducted on registered collections by PDs according to a schedule of audits (peer-to-peer audits). See SOP HTA006: Quarantine, Registration and Audit.

### 3.3.3 A local SOP for internal audit must be followed.

### 3.3.4 Audit should be a formal, documented process undertaken by a trained, objective person who has no vested interests in the audit results. As such, staff should not be auditing their own work; where possible, colleagues should audit each other’s work.

### 3.3.5 Internal audits should include:

a) Traceability audits (vertical audits) of records and specimens to provide assurance that the process for tracking and tracing samples, from the point of receipt through to the point of release for research or eventual disposal, is robust and consistent with the HTA Traceability Standards, according to the principles detailed in core Traceability SOP (HTA002). A template form for traceability audits (HTA_FRM004) is available from the HTGT.

b) Horizontal audits to ensure that SOPs are reflected in actual practices. See HTA TEMP019 Template internal audit form.

c) Audits of records for completeness, accuracy and legibility (e.g. consent records, temperature logs, etc.).

### 3.3.6 Audit findings must be documented and include corrective actions if applicable, detailing who is responsible for implementing these actions and a timeline for completion. Each audit must be brought to a conclusion by completing any follow up actions and recording the final outcome in an audit report. Collection custodians can thereby provide evidence that appropriate corrective and preventive actions have been taken to address audit findings.

### 3.3.7 If audit findings require corrective actions, a follow-up audit must verify that corrections were made and corrective actions were taken. This is described as closing the audit cycle.

### 3.3.8 Report any adverse events / incidents or non-conformities relevant to HTA licensed activities discovered during internal audits to the DI and HTGT, following procedures detailed in core SOP HTA003 Incident Reporting.

**NOTE 6:** The GCP Training for Clinical Trials of Investigational Medicinal Products (CTIMPs) includes a module on Monitoring, Audit, Reports and Ongoing Responsibility. Audit training outside of the GCP training may be arranged by contacting the HTGT.

**NOTE 7:** The HTGT have a monitoring, mediation and oversight role, with the emphasis being on training for audit and problem solving for difficult issues. To ensure that
shortfalls are not left as breaches / non-conformities for unacceptable periods of time, there is a process for escalating problems identified during audit as outlined in 5.2.

3.4 Staff training

3.4.1 Records must be kept of staff qualifications and all training received by all personnel working under the licence.

3.4.2 Staff must be able to demonstrate knowledge of regulatory requirements, internal policies and procedures for licence 12217, University policies and procedures, as well as any local policies and procedures relevant to the collection(s) they are involved with.

3.4.3 All staff working under the licence must receive documented training on the HT Act, HTA Codes of Practice and Standards, including licensing requirements. This is provided online via the WebLearn Platform and access is controlled by the Oxford Single Sign On. This training is mandatory for anyone declaring (via the annual Human Tissues Declaration which is organised via PDs and Departmental Administrators) that they have anything at all to do with working with human tissues.

NOTE 8: Monitoring of completion of the training by staff will be carried out by the HTGT. Certificates will be issued by the HTGT to staff who have passed the WebLearn training for inclusion in their training records.

3.4.4 Persons working under the licence will be required to update their training on WebLearn once every two years.

3.4.5 Training on licence core SOPs will be provided by the HTGT upon release of new documents or amended versions.

3.4.6 Documented induction training programmes must be in place to train new staff and must include the WebLearn training on the HT Act and the HTA if the new member of staff will be undertaking any work with human tissue.

3.4.7 Training provisions for new staff working with samples registered under licence 12217 must include training on and acknowledgement of the licence core SOPs as described in section 3.2.9.

3.4.8 Training provisions must be extended to visiting staff.

3.4.9 Mechanisms for recording training include:
   a) Acknowledgement of new documents or amended documents, either electronic or on paper
   b) Competency assessments
   c) Records of training on procedures
   d) Completion of induction programme(s)
   e) Certificates from formal training courses or programmes, including online courses
   f) Learning logs
g) Details of attendance at conferences and workshops
h) Personal training logs.

3.4.10 Training packages including induction programmes must be reviewed at regular interval.

NOTE 9: The University Training and Personal Development Review (PDR) scheme is in place for all staff. The HTA expects that staff have appraisals and personal development plans.

3.5 Risk management

3.5.1 Documented risk assessments must be in place for all practices and processes requiring compliance with the HT Act and HTA’s Codes of Practice, and must include sufficient details of the risks and mitigating actions. In addition to a set of core Risk Assessments for activities conducted across the licence, local risks assessments must be in place for specific activities.

3.5.2 Assessment of risk may be appropriate to be carried out at departmental, institute or building level, in which case a documented copy of the assessment should be made available to all relevant staff.

3.5.3 When documented risk assessments are in place, there should be a clear procedure for allowing staff to access these documents. There should be documented staff training on the risks and mitigating actions relating to activities conducted under the licence, in order to provide evidence that staff are informed.

3.5.4 Regular review of risk assessments is mandatory. The risk assessments should be reviewed every three years at a minimum; in addition, a review of relevant risk assessment(s) must be conducted following an adverse event.

3.5.5 Risks assessments must be included in the document control system to ensure staff are accessing the latest version.

3.5.6 Departmental PDs are responsible for the review of activity-specific risk assessments for compliance with requirements.

3.5.7 Regular audits of risk assessments and their reviewing will be part of the peer-to-peer audit process (see core SOP HTA006®).

3.5.8 Risk assessments must include at a minimum:
   a) An evaluation of risks, including Health and Safety risks as well as risks related to regulatory compliance such as:
      i. Receiving or storing samples without appropriate consent documentation
      ii. Storing or using human tissue after consent has been withdrawn
      iii. Storage failure or other damage affecting tissue quality for research
      iv. Loss of human tissue
      v. Sample mix-up or loss of traceability

Adapted from CTRG Template SOP Version 2.1
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vi. Risks related to the transportation of specimens to or from the establishment

vii. Breaches of security

viii. Incorrect disposal

ix. Breaches of confidentiality or data protection

b) The level of risk (low, moderate, high risk) before implementation of mitigating actions

c) Details of mitigating actions taken to minimise the risk

d) Any residual level of risk after mitigating actions have been implemented.

NOTE 10: Guidance on conducting risk assessments can be found on the University of Oxford’s Safety Office website.

3.6 Adverse events

3.6.1 Incidents relating to HTA licensed activities must be reported consistently to the DI and HTGT according to the Core SOP for Incident reporting (HTA003) within 4 days. This is to ensure the DI retains oversight of all such incidents.

3.6.2 All personnel working under licence 12217 must be instructed on how to use incident reporting systems; this includes incident reporting at the level of the HTA licence, but also any local incident reporting procedures, University or NHS Trust procedures, as well as any additional reporting requirements.

3.6.3 Induction programmes should contain instructions on the procedures to follow in case of an incident and how to record non-conformities.

3.7 Management of records

NOTE 11: Records may include for example: consent records, inventories and manifests, tissue requests, MTAs, tissue transfer logs, courier slips, temperature or calibration logs, cleaning logs, disposal logs etc. The format of these records may be paper-based or electronic.

3.7.1 Systems for the creation, amendment, retention and destruction of records must be documented in SOPs.

3.7.2 Forms and logs must be reviewed periodically; the frequency of review required should be documented to ensure they are updated regularly.

3.7.3 Back-up and recovery provisions should be in place where possible, and documented in a SOP.

3.7.4 Systems ensuring data protection, confidentiality and public disclosure to comply with the Data Protection Act 1998 must be in place and documented in a SOP.
4. INTERNAL AND EXTERNAL REFERENCES

4.1 Internal References

1. HTA Licence Constitution (HTA008)
2. CTRG core SOPs and SOP template:
   https://researchsupport.admin.ox.ac.uk/ctrg/resources
3. HTA Licence Policy (HTA007)
4. Licence 12217 Quality Manual (link to follow)
5. WebLearn site for training on the HT Act, the HTA standards and codes of practice and for electronic acknowledgement of new documents and versions:
   https://weblearn.ox.ac.uk/portal/site:/medsci:hta/tool/8d799d02-a109-4536-8e3b-85ed6f6c1170
6. HTGT core SOP on Quarantine, Registration and Audit (HTA006)
7. HTGT core SOP on Traceability (HTA002)
8. Traceability audit form (HTA_FRM004) (link to follow)
9. Template internal audit form (HTA_TEMP019)
10. HTGT core SOP on Incident Reporting (HTA003)
11. GCP training:
    https://researchsupport.admin.ox.ac.uk/ctrg/training
12. University of Oxford Safety Office information on risk assessments:
    https://www.admin.ox.ac.uk/safety/policy-statements/s5-08/

4.2 External References

1. Human Tissue Act 2004:
   http://www.legislation.gov.uk/ukpga/2004/30/contents
2. Relevant material information from the HTA:
3. HTA Research standards and guidance:
   https://www.hta.gov.uk/standards-and-guidance
4. ISO 9001:
5. **APPENDICES**

5.1 **Overview of licence documentation**

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**Policy**

**Core documents**

- Core SOPs
- Core Risk Assessments
- Quality Manual

**Departmental or local documents**

- Local SOPs
- Local Risk Assessments
5.2 Process for problem solving following local audits

- PD agrees plan with PI to remedy shortfall
- If progress not sufficient, DI and HTGT provide mediation
- If progress still not sufficient, involve Head of Department and DI in finding a solution