Internal Auditing Procedure for Research Tissue Banks

NJRO-TISS-SOP-004

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1. Background/Introduction

Newcastle University and Newcastle Hospitals each hold a research sector Human Tissue Authority licence (ref. 12534 and ref. 12193, respectively). This licence authorises the storage of "relevant material" (material, other than gametes, that consists of, or includes human cells) which has come from a human body for research in connection with disorders, or the functioning, of the human body.

All relevant material which is being stored for use in future research projects must be stored under the appropriate establishments Human Tissue Authority licence, unless a suitable exemption exists – for example, if there is current NHS National Research Ethics Service (NRES) Research Ethics Committee (REC) approval in place to use the samples. Note – University Ethical Approval is not exempt from requiring storage under the licence.

In Newcastle, relevant material is stored for research purposes in a number of pre-approved locations within Newcastle University and Newcastle Hospitals premises. Material is stored under the approval of NHS REC approved research tissue banks, or in non-NHS REC approved biobanks (under which project specific REC approval would be required for further use of the samples).

Internal audits of research tissue banks in Newcastle aim to assess compliance with:

- The Human Tissue Act (2004) regulations, associated Codes of Practice and licensing standards.
- Terms and Conditions of ethical approval granted by a REC (NHS REC approved research tissue banks).
- Internal systems e.g. institutional policies and procedures, any requirements set by the Designated Individual (DI) named on each establishments Human Tissue Authority licence.
- General Data Protection Regulations (GDPR) and Data Protection Act 2018

This aims to support researchers to identify any gaps in compliance and enable solutions to be identified and implemented to meet regulatory standards.

2. Purpose

The purpose of this SOP is to provide information to all personnel working under the Newcastle University or Newcastle Hospitals Human Tissue Authority licence, on the internal audit procedure adopted by the Newcastle Joint Research Office to ensure

compliance with core standards relating to the storage of samples and associated clinical data for human tissue research.

3. Scope of Document

This SOP applies to any personnel working under the Newcastle University or Newcastle upon Tyne Hospitals (NUTH) Human Tissue Authority licence. This includes Persons Designated, Chief Investigators of NHS REC approved research tissue banks, and local collaborators (e.g. Principle Investigators, laboratory staff, tissue collection centres).

NHS REC approved research tissue banks which only store non-relevant (non-cellular material, such as DNA or cell lines) are also subject to audit under the same procedures, due to the requirement to be stored on Human Tissue Authority licensed premises, and to ensure the same high standards are applied.

This does not apply to Good Clinical Practice (GCP) studies and studies with current NHS Research Ethics Committee approval as these are audited separately in line with NJRO-QA-SOP-001.

4. Definitions

Auditee	The person representing the institute/system being audited responsible for hosting the audit and responding to any observations raised
Auditor	A person independent from the institute, or person specifically tasked by the institute, responsible for undertaking the audit and raising the observation
CAPA	Corrective Action, Preventive Action
Designated Individual (DI)	The person named on a licence issued by the Human Tissue Authority, under whose supervision licensed activities are carried out. The DI has a statutory responsibility to ensure that those carrying out licensed activities, and their practices, are suitable, and that the conditions of the licence are met.
GDPR	General Data Protection Regulations
HT Act	Human Tissue Act
HTA	Human Tissue Authority

IRAS	Integrated Research Application System
MTA	Material Transfer Agreement
NJRO	Newcastle Joint Research Office
NRES	National Research Ethics Service
NUTCRI	Newcastle University Translational Clinical Research Institute
NUTH	Newcastle upon Tyne Hospitals NHS Foundation Trust Hospitals
Persons Designated (PD)	Person, as notified to the HTA for the Licence, who directs others in relation to the HT Act within the institute
QMIF	Quality Management Improvement Forum
REC	Research Ethics Committee
Relevant Material	Material, other than gametes, that consists of, or includes human cells
R&D	Research and Development
SOP	Standard Operating Procedure

5. Roles & Responsibilities

It is the responsibility of:

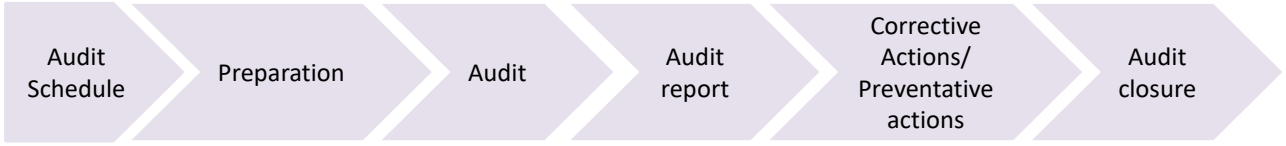
- The NJRO Quality Management team to issue audit reports and certificates and compile audit schedules.
- All research staff operating under the research sector Human Tissue Authority licence to store material in compliance with the Human Tissue Act (2004), research ethics and General Data Protection (GDPR) regulations, and make themselves available for audit at any time.
- The NJRO Quality Management team (or approved, trained delegate) to conduct human tissue audits. It is the responsibility of auditees to review audit reports and provide any feedback. It is the responsibility of audit approvers to review and sign audit reports.
- Auditees to complete appropriate corrective and preventative actions tables within an agreed timeframe, and complete these actions as set out in the tables.

6. Procedures

Internal research tissue bank audits are typically conducted by the Newcastle Joint Research Office (NJRO) Quality Management team, however other suitably trained individuals may conduct these audits when required.

Internal auditors must not be involved in auditing their own work. Audits must be undertaken by a person not normally involved in the activity requiring audit. Audits may however be conducted within departments as part of a "self-inspection" programme to assess performance against internal, external and regulatory standards.

The format of these internal audits is set out below.



6.1. Audit Schedule

Audits of all Newcastle University biobanks are typically conducted every 2 years by the NJRO, where feasible. Frequency of audit will be reviewed on an annual basis as part of the audit schedule planning and may be increased or decreased on a risk basis. In addition, self-assessment audits should be conducted by the research tissue banks. For further information, see section 6.7.

At the beginning of the calendar year an audit schedule will be compiled by the NJRO Quality Management team working in collaboration with the Designated Individual on each Human Tissue Authority licence. Efforts will be made to reduce the audit burden on researchers by rationalising audit agendas within the Quality Management team and collaborating, where possible.

Auditees must confirm who will attend each audit and ensure the availability of all required staff. It is vital that all key staff attend the audit to ensure that all areas requiring audit can be addressed on the day, where possible. If staff can no longer attend, the auditor should be contacted to reschedule. Audit duration will vary dependent on the size and complexity of the group.

Once dates have been agreed, the audit schedule is finalised and presented to the DI for approval as part of the annual governance review. Dates for audits are subject to change, and may be updated throughout the year based on any staff changes, resource or change in processes.

In addition, further areas for audits may be identified throughout the year – for example, consent form audits, or new research tissue banks. These will be scheduled as required. Any changes to the audit schedule will be agreed with the NJRO Quality Management team, and the audit schedule updated.

6.2. Preparation for audit

In advance of the audit, the auditor will provide the auditees an audit agenda, detailing the proposed structure and aims of the audit. The audit agenda will vary depending on the reason for the audit, the size/scale of the group, type of collection and any perceived risk. Auditees will be offered the opportunity to add to the agenda, if required.

Auditees will also be provided with a list of documents/information required in advance of the audit. This may include:

- A pre-audit questionnaire (NJRO-TISS-T-009) – Detailing total numbers of relevant material held by the bank, storage details etc.
- Associated paperwork e.g. ethics documentation, such as copies of IRAS applications, approval letters, substantial amendments, access policy and conditions of approval of the bank
- A copy or list of quality documents associated with licensable activities (e.g. SOPs, policies, forms, risk assessments)
- A staff list
- Blank consent forms/patient information leaflets
- Copies of any MTAs or supply agreements used by the bank.

Other documents may be provided as information for the auditee, or requested by the auditor as further information relevant to the audit process, as appropriate.

Auditees must ensure the Human Tissue Master File is up to date, in accordance with NJRO-TISS-SOP-010.

The agenda will be provided at least 2 weeks before the audit, to allow the auditee's time to prepare. If this is not feasible for any reason (e.g., urgent audit) and an agenda is provided with less notice, the auditees will be asked if they are happy to go ahead.

Where appropriate, an audit pre-meeting may be requested by the auditor, or auditee. A pre-meeting is used to discuss any information required prior to the main audit, to support auditees in preparing, or to agree the approach to audit in complex situations.

Auditees must ensure that all research tissue bank documentation is made readily available for audit on the day (including access to paper and electronic records). This includes:

- Sample tracking records
- Sample transfer documents (e.g. MTAs, courier paperwork)
- Up to date Human Tissue Master File
- Standard Operating Procedures, Policies, Work instructions etc.
- Ethics documentation
- Staff training records
- Equipment maintenance and recording records

6.3. Audit Conduct

6.3.1. Opening meeting.

The audit will commence with an opening meeting, chaired by the auditor. It is important that all key staff attend this meeting. The aim of the opening meeting is to introduce the audit, go through the audit agenda for the day, any documentation that will be used, and requirements of staff.

There will also be the opportunity to highlight any proposed changes to the agenda (e.g. if any members of staff are off sick/unavailable, or certain aspects have to be rescheduled).

The audit will then begin, in accordance with the audit agenda. Members of the research group who are not involved in certain aspects of the audit may leave until required.

6.3.2. Audit structure

Audits will be conducted using appropriate audit checklists. The following checklists may be used

- Human Tissue Master File Audit Checklist (NJRO-TISS-T-004)
- NRES REC Approved Research Tissue Bank Management Audit Checklist (NJRO-TISS-T-005)
- Human Tissue Audit Checklist (NJRO-TISS-T-006) – Used to facilitate audits of Research Tissue Banks operating without ethical approval, and NRES REC Approved research tissue bank studies.
- Consent Form Audit Checklist (NJRO-TISS-T-007)
- Sample traceability audit checklist (NJRO- TISS-T-008)

These check lists have been created to ensure all regulatory standards are appropriately assessed.

6.3.3. Auditing Standards

For material stored under the Human Tissue Act, compliance will be assessed against Code of Practice A (Guiding Principles and the fundamental principles of consent) the four HTA licensing standards applicable to the Research Sector, and derived from Code of Practice E, Research. For a copy of the Codes of Practice, refer to the HTA website.

1. Consent
2. Governance and Quality Systems
3. Traceability
4. Premises, Facilities and Equipment

A copy of these licensing standards, including guidance to support compliance, can be found on the Human Tissue Authority website: https://www.hta.gov.uk/

For NHS REC approved Research Tissue Banks, banks are also audited for compliance with the Terms and Conditions of ethical approval, as granted when the bank was established.

For studies conducted under the ethical approval of an NHS REC approved research tissue bank, compliance will also be assessed with the banks documented policies and procedures (e.g. Access Policy, SOPs).

Audits will also assess compliance with the principles of the General Data Protection Regulations (GDPR) and Data Protection Act (2018).

All audits will assess compliance with institutional policies and procedures (e.g. safety office, and University or Designated Individual mandates), Newcastle Joint Research Office (NJRO) policies and procedures and local policies and procedures. For more information on the Quality Management system adopted to support human tissue research in Newcastle, please refer to

- Newcastle University Quality Manual (NJRO-QA-POL-001)
- Newcastle Hospitals Quality Manual (NJRO-QA-POL-002).

6.3.4. Audit closure

Following completion of the audit, a closing meeting/discussion will be held to summarise the audit activities, to recognise good practice and discuss any observations and possible corrective actions. Any further follow up audits (e.g. collections audits, consent form audits) will be agreed, including the contact details of those who must be contacted to arrange the audits.

6.4. Audit report

An audit report will be issued within four weeks of the audit detailing the inspection observations and recommended corrective/preventative actions. Where the report may take longer (e.g. due to further investigations, or follow up audits), auditees will be informed. Any critical findings must be approved by the NJRO Quality Management Improvement Forum (QMIF) prior to issue of the report.

Audit reports will be written in sufficient detail to thoroughly document the audit discussions and findings. An executive summary will be provided to summarise the audit. Where a subsequent audit has identified as being required, this report will be written up and provided separately, with no duplication of findings between the reports.

Where information is added post audit (e.g. by way of an update/clarification) this will be clearly noted. Wherever possible, references will be provided to the appropriate regulatory standard to which the finding relates. Where any findings are made that relate to other standards (e.g. Good Clinical Practice) the Quality Management team in the NJRO will be informed to ensure these can be investigated separately.

Audit findings will be categorised in accordance with the Human Tissue Authority approach to auditing (see table 1, overleaf). Note: Findings which relate to other regulations (e.g. research ethics, GDPR) will be categorised in the same way, with further explanatory notes, where required. If findings are noted in relation to other standards (e.g. GCP) these will be recorded as “other” in order to allow these to be flagged for information (e.g. for the NJRO Quality Management team GCP audits to further investigate).

Recommendations on how to address audit findings will be provided by the auditor in the audit report. These recommendations should be used to facilitate the completion of the Corrective Actions/Preventative Actions (CAPA) table which must then be completed by the auditee(s) in response to the report.

Auditees must complete the auditee table at the back of the report, including any comments (e.g. To highlight any errors/omissions) and confirmation of who has completed the CAPA table (see section 6.5). Note - Where there are multiple auditees, only one set of comments from all auditees is to be received. This will be reviewed by the NJRO Quality Management team and if required, amendments made.

For more complex discussions or escalation of any issues, a follow up post-audit meeting may be required. Where comments are not considered to be valid, the auditor reserves the right to issue the report without any changes. Any issues may be escalated via the Newcastle University Translational Research Institute (NUTRCI) Executive Board.

Table 1: Categorisation of findings under the Human Tissue Act (2004)

Category	Description
Critical shortfall	A shortfall which poses a significant risk to human safety and/or dignity or is in breach of the Human Tissue Act 2004 or associated directions Or - A combination of several major shortfalls, none of which is critical on its own, but which together could constitute a critical shortfall and should be explained and reported as such.
Major shortfall	A non-critical shortfall that • Poses a risk to human safety and/or dignity, or • Indicates a failure to carry out satisfactory procedures, or • Indicates a breach of the relevant codes of practice, the Human Tissue Act, and other professional and statutory guidelines, or • Has the potential to become a critical shortfall unless addressed Or - A combination of a number of minor shortfalls, none of which is major in its own right, but which together could constitute a major shortfall and should be explained and reported as such.
Minor shortfall	A shortfall which cannot be classified as either critical or major, but which indicates a departure from expected standards/good practice.
Other	Where a shortfall has not been identified, but areas for improvement have been identified, leading to the auditor providing advice to the auditee on improvements. Or Where findings relate to non-HTA findings, such as relating to the National Research Ethics Service (NRES) Research Ethics Committee approval or R&D requirements.

6.5. Corrective Actions/Preventative Actions (CAPA)

The auditee must respond to audit findings within the timeframe stipulated within the report when issued. A completed CAPA table must be provided, detailing the action plan to address audit findings, identifying the individuals/groups responsible for completing these actions, and expected completion dates. The CAPA table must be approved by the auditor as an appropriate course of action.

In instances where the report sign off is delayed (e.g. due to discussions) the final CAPA table should be provided within a 4 weeks of the final report being issued, unless an extended timeframe is agreed with the auditor.

Where complex observations require a more detailed response, or in agreed exceptional circumstances, a longer period may be assigned, with the agreement of the auditor and/or Designated Individual. In the event of a response not being issued within the time, a position statement, detailing the reasons why and the expected time frame for completion should be forwarded to the auditor.

The NJRO Quality Management team will keep a log of all audit findings and CAPA, with reminders for completion. As each action is completed, the action taken, completion date and person completing the action should be documented and the information provided to the auditor. The auditor may also request a further audit of the facility to confirm that corrective actions have been implemented.

6.6. Audit closure

On completion of an appropriate corrective and preventative actions table and signature of the final report by the auditees, the audit will be considered complete.

Reports will be approved by the relevant institutional Designated Individual. In instances where the DI is the auditee (e.g. Research Tissue Bank Chief Investigator) these will be peer reviewed by a member of the NJRO QA Management Team.

Signatures may be electronic or wet-ink signatures. Once finalised, a PDF version of the final report will be sent to auditees and an audit certificate issued.

Internal audit reports will be treated as confidential and not be shown to outside organisations unless required as part of regulatory inspections, or prior approval has been granted by the group. A summary of all audit findings will be presented annually to the

Dean of Translational Research as part of a governance review. All audit findings will be used to populate a risk register from which annual audits will be prioritised.

6.7. Self-assessment audits

In addition to formal audits conducted by the NJRO Quality Management team, research tissue banks must also conduct regular self-assessment audits for regulatory compliance. These should be used to identify any areas for improvement or gaps in compliance. These should be formally documented and made available as part of internal audits. Researchers are recommended to utilise the audit checklists (see section 6.3.2) to facilitate self-assessment audits.

6.8. Human Tissue Risk Assessments

In order to assess risk in relation to compliance with the Human Tissue Act (2004) standards and associated Codes of Practice, a new Human Tissue Risk Assessment will be introduced in 2019. This must be completed/reviewed and reissued following audits in order to reassess risk and ensure continuous process improvement. Where required, key staff within research tissue banks will be requested to help complete these assessments.

7. References

www.hta.gov.uk

Code of Practice A – Guiding Principles and the fundamental principles of consent

Code of Practice E: Research