Adverse Event Reporting under the Newcastle University, and Newcastle Upon Tyne Hospitals Human Tissue Authority research sector licences

NJRO-TISS-SOP-003

Contents

1. **Background/Introduction**
2. **Purpose**
3. **Scope of Document**
4. **Definitions**
5. **Roles & Responsibilities**
6. **Procedures**
7. **References**
8. **Appendices**

1. Background/Introduction

Newcastle University and Newcastle Upon Tyne Hospitals (NuTH) holds a research sector Human Tissue Authority licence (ref. 12534, and 12193 respectively). The licences authorise 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. Material is stored in Newcastle on behalf of internal researchers and for external clients/collaborators and in NuTH, material is stored for release to both internal and external researchers.

It is a licensing requirement to have a system in place to ensure that all adverse events associated with the procurement, testing, processing, storage and distribution of human tissue and cells are investigated promptly and corrective and preventative actions taken where required. Staff must be instructed on how to use the incident reporting system and effective corrective and preventative actions must be taken where necessary and improvements in practice made.

2. Purpose

The purpose of this SOP is to provide staff working under the Newcastle University and NuTH research sector Human Tissue Authority licences with information on recording, managing, and reporting Adverse Events relating to human tissue stored under each establishments Human Tissue Authority research licence.

3. Scope of Document

This SOP applies to any personnel working under the Newcastle University and NuTH research sector Human Tissue Authority licences (ref. 12534 and 12193 respectively). This includes Persons Designated, Chief Investigators of National Research Ethics Service (NRES) Research Ethics Committee (REC) approved research tissue banks, and local collaborators (e.g., Principal Investigators, laboratory staff, tissue collection centres).

This does not apply to adverse events related to:

- Non-relevant material (i.e., human material considered to be out with the scope of the Human Tissue Act).
- Clinical Trials of Investigational Medicinal Products (CTIMPs) and trials of Advanced Therapy Medicinal Products (ATMPs). The procedure to follow for the recording,

managing and reporting of adverse events for CTIMPs, ATMPs and non ATMP studies is found in NJRO-REG-SOP-007 and NJRO-GOV-SOP-005, respectively.

If it is believed that an adverse event relates to personal data breach under the General Data Protection Regulations, this must be reported separately, in accordance with Newcastle University procedures – accessed via the staff homepage. In addition to the reporting system set out in this SOP, Newcastle Upon Tyne Hospitals Trust requires that all incidents including HTA related adverse events be reported using the Datix Cloud IQ (DCIQ) system via the NuTH staff intranet page.

4. Definitions

Adverse Event (AE)	Any untoward occurrence associated with the procurement, testing, processing, storage and distribution of human tissue or other human materials that lead to or had the potential to lead to: • the loss or damage of stored human tissue • the harm to staff or visitors • a breach of security of the premises and the contents contained therein • a breach of the Human Tissue Act or the Code of Practice • the need for an internal inquiry
Adverse Event Report (AER)	The system used to report adverse events
ATMP	Advanced Therapy Medicinal Products
Corrective Action/ Preventative Action (CAPA)	Actions that are identified during the investigation into the adverse event that either act to: • Correct the current issue through remedial action, or • Prevent the event occurring again
CTIMP	Clinical Trials of Investigational Medicinal Products
GDPR	General Data Protection Regulation
Designated Individual (DI)	The individual designated on the Licence to supervise the licensable activities carried out. DIs are trained by the Human Tissue Authority to perform this important role and they have statutory responsibilities they must fulfil

Human Tissue Authority (HTA)	The governing body set up to regulate activities that come under the Human Tissue Act
NJRO	Newcastle Joint Research Office
Persons Designated (PD)	A person named on the Human Tissue Act licence who supports the Designated Individual by directing others in relation to the Human Tissue Act within their local environment
Principal Investigator (PI)	The appropriately qualified individual at each project site who has responsibility for the conduct of the project at that site

5. Roles & Responsibilities

It is the responsibility of all staff operating under Newcastle University, and NuTH research sector Human Tissue Authority licences to ensure adverse events relating to human tissue samples are investigated and reported in line with this procedure, in a timely manner.

It is the responsibility of these staff to identify appropriate corrective and preventative actions, where required, and act on these within agreed timeframes.

It is the responsibility of the NJRO Quality Management team to audit compliance with these procedures.

6. Procedures

The procedure for recording, managing, and reporting Adverse Events under a research sector Human Tissue Act licence is summarised in figure 1:

Figure 1: Adverse event report process

This process is documented below.

6.1. Identifying an adverse event

The Human Tissue Authority defines an adverse event as:

- any event that caused harm or had the potential to cause harm to staff or visitors
- any event that led to or had the potential to lead to a breach of security of the premises and the contents contained therein
- any event that caused harm or had the potential to cause harm to stored human tissue (including loss)
- any other event that gave rise to an internal inquiry any breach of the HT Act or the Code of Practice

Any personnel working with human samples should therefore be vigilant and alert to recognising actual or potential adverse events and are encouraged to identify any incident they believe may compromise compliance with the licensing obligations under the Human Tissue Authority licence. Examples of adverse events are provided in Table 1, overleaf.

It should be noted that this is not an exhaustive list, as any incident that has a potential impact on the integrity of the stored tissues or cells, or the procurement for storage should be considered. This includes “near-miss” situations, whereby an adverse event could have occurred if intervention had not been made.

Further advice on the identification of an adverse event may be sought from the Newcastle Joint Research Office (NJRO) Quality Management team.

Table 1 – Examples of Adverse Events

TYPE OF INCIDENT
Consent
• Human tissue removed from patient without appropriate consent. • Human tissue stored without appropriate consent. • Human tissue used without appropriate consent. • Human tissue used for research project that has not been REC approved. • Staff member seeking consent is not appropriately trained
Governance
• Conduct of non-licensed activities • Wrong version of SOP in use/failure of change control mechanisms • Breach of data protection/confidentiality (e.g., sample bearing patient identifiers) • Research material sent off site without a Material Transfer Agreement (MTA)
Sample taking
• Wrong type of specimen • Incorrectly labelled specimen • Specimen from wrong patient • Specimen in wrong format
Tracking
• Labelling error • No record of stored sample on tissue database • Sample logged on tissue database but not in correct location. • Incomplete audit trail resulting in failure to trace sample. • Tissue database failure
Storage
• Short term cold storage failure • Alarm failure • Cold storage failure and alarm failure resulting in material loss. • Any other event which compromises tissue integrity
Transportation
• Sample lost in transport. • Sample integrity compromised in transport
Disposal
• Failure to dispose of material appropriately. • Incorrect labelling of human tissue waste • Failure to document reason for sample disposal.

6.2. Investigating an Adverse Event

Once an adverse event has been identified and confirmed to not be a false alarm it should be investigated immediately using the "Internal Investigation Checklist" (NJRO-TISS-T-002) to establish the root cause, and identify any potential corrective or preventative actions.

The investigation should be commenced as quickly as possible following the identification of the adverse event - ideally within the same working day. The Person Designated (PD) for the local area (or nominated individual) should be promptly informed and involved where necessary.

Following the completion of this investigation, the adverse event should be reported.

6.3. Reporting an Adverse Event

Following the investigation into the root cause of the adverse event, a report should be compiled using the "Adverse Event Report" template (NJRO-TISS-T-003). Alternative templates may be used providing they capture sufficient information to detail the event. This will be determined by the NJRO Quality Management team.

Reports should clearly describe the event, explaining the facts, and be written in a format suitable to be understood by individuals not familiar with the group's internal procedures (e.g., Lay Member of an Access Committee, NJRO Quality Management team, Licence Holder).

It should be considered that the report may be read by a client, regulator, or other party external to the group (where appropriate). Therefore, reports should avoid acronyms, slang, or assign blame, but clearly state the facts, and order of events in appropriate language.

Newcastle University must inform the client of any major quality incident or non-conformance involving their samples within 14 calendar days of the incident occurring or non-conformance being identified – unless alternative arrangements have been made with the customer. A copy of Newcastle University's adverse event report must be made available to the customer within thirty days of the adverse event being discovered.

The procedure for compiling an "Adverse Event Report" is provided below.

6.3.1. Adverse Event Details

Using the investigation checklist, the details of the event should be reported, including:

- The name of the Biobank affected, the Research Ethics Committee (REC) number (if applicable) and the Person Designated responsible for oversight of the samples.
- The date/time of the adverse event (if known) and when it was observed.
- The name of the person reporting the adverse event, and who it was reported to.
- The location where the adverse event has occurred. This must include as much detail as possible e.g., the building name, room number, freezer number etc.
- The type of incident, as determined using Table 1. Where it is believed that the type of incident is not clearly assigned to one or more category, further information should be provided.
- A description of the adverse event including the perceived root cause of the problem. This should be completed clearly, in as much detail as possible, with consideration that this may be viewed by individuals not familiar with the group's procedures (e.g., Lay person, Client).
- Information on any immediate corrective actions conducted.
- Where "relevant material" under the Human Tissue Act is affected, this must be stated. Where a researcher is unclear of whether the material constitutes relevant material, they should consult the Human Tissue Authority Website – www.hta.gov.uk.
- Where sample integrity has been compromised this should be described, including as much detail as possible on the samples affected (e.g., sample numbers, box number, or list of samples, as appropriate). A sample inventory should be provided with the report. Where investigations have been/are to be conducted to assess sample integrity, details of these investigations should be provided.

6.3.2. Risk and Impact Assessment

A risk assessment should then be conducted for the adverse event based on three factors:

Table 2: Impact assessment

		Risk category	Risk score
Severity of harm	The perceived significance of the adverse event based for example on the ethical implication, effect on other samples, or non-compliance with regulations	High	5
		Medium	3
		Low	1
Probability of reoccurrence	The perceived probability of the adverse event occurring again without corrective/preventative action	High	5
		Medium	3
		Low	1
Likelihood of detection	The likelihood that if the event were to occur again, that it would be quickly and easily detected	High	1
		Medium	3
		Low	5

Together these three factors should be used to perceive the overall impact of the adverse event, by calculating the total impact score - calculated as:

Risk score = Severity of harm x Probability of re-occurrence x Likelihood of detection

Risk scores ratings:

Score	Impact Assessment
1-5	Low
6-15	Medium
16-25	High

The impact of the risk should then be summarised in the impact assessment box, detailing any factors that may have been affected e.g., ethics, compliance.

Based on the perceived impact of the adverse event, the event should be categorised based on severity as “serious”, “moderate”, “minor”, or “near miss”. Categorisation should be considered as part of a risk-based approach and the NJRO Quality Management Team consulted where required. However, it should be noted that:

- All potential adverse events should be considered serious until proven otherwise.
- Near-miss adverse events should be managed in the same way as adverse events which have actually occurred, to ensure that corrective action can be put in place to ensure that an adverse event does not occur in the future.

Examples of these classifications are provided in table 3.

Table 3: Examples of categorisation of adverse events

Category	Example of adverse Event
Serious*	• Conduct of non-licensed activities • Non-recoverable loss of unique relevant material (e.g., through freezer/alarm failure) • Relevant material removed from a participant, stored, or used without appropriate consent. • Staff member seeking consent without appropriate training. • Loss/compromise of relevant material and/or patient records during transportation • Relevant material used for a research study without NHS REC approval. • Breach of Data protection/confidentiality • Failure to dispose of material appropriately
Moderate	• Relevant material transported without appropriate transfer agreement (e.g., MTA, SLA) in place. • Labelling error that led to the incorrect use of samples • Inappropriate transport of specimens • Freezer failure leading to the requirement to transfer samples to alternative locations.
Minor	• Incorrect version of policy or SOP in use • Not registering new SOPs or updating existing SOPS to reflect changes in practice. • Documentation temporarily misplaced
Near Miss	An adverse event could have occurred if intervention had not been made, e.g. • Short term cold storage failure • Alarm failure • Labelling error that was remedied

Note to table:

- Customers of the Biobank will only be informed of serious adverse events, unless otherwise deemed necessary.
- Where required, the DI is responsible for ensuring that serious adverse events are reported to the Human Tissue Authority.

6.3.3. Informing relevant parties

The adverse event report should also be updated to include any relevant parties that need to be informed of the event e.g., the Sponsor, regulator, customer etc. Where the need to share this information is unclear, this should be discussed with the NJRO.

Where the relevant parties have already been informed, this should be indicated in the table, and evidence of the communication (e.g., printed email trail) attached to the report as an appendix for review.

6.3.4. Corrective Actions/Preventative Actions ("CAPA")

Based on the findings from the root cause analysis, a Corrective and Preventative Actions (CAPA) table should then be populated, detailing the findings, CAPA to be completed, a date for completion, and action owner, to ensure that a clear action plan for remedial action is identified.

6.3.5. Approval

All adverse event reports must be signed by the individual reporting/investigating the event and the Person Designated (or delegate) for the local area. For departments which wish to add additional signatories (e.g., Biobank Manager, research tissue bank manager, or local Quality Assurance Manager), these should be added as appropriate, detailing the individual's name, and role description.

The form should then be passed promptly to the NJRO Quality Management team for review and approval. For adverse events relating to the Human Tissue Act, the Designated Individual must also sign the report.

Where required a copy of the Adverse Event Report will also be sent to the Customer for approval. In instances where the Customer is unsatisfied with the investigation, the Intellectual Property & Legal team should be consulted.

Fully executed Adverse Event Reports (AER) will be scanned and uploaded into a secure folder overseen by the NJRO Quality Management Team. Copies will be sent to the team responsible for reporting the event, and the Designated Individual. Further individuals may be sent the report, as required (e.g., Licence Holder, NJRO or Faculty Management teams), for example, for escalation, or for reporting purposes. Actions added for corrective or preventative actions to be completed. A log of adverse events will be retained by the NJRO Quality Management Team, including a list of agreed CAPAs (see section 5.4).

6.4. Completing Corrective Actions/ Preventative Actions (CAPA)

Corrective and preventative actions should be completed in the agreed timeframe, unless otherwise negotiated with the NJRO Quality Management team and/or client, as appropriate.

It is the responsibility of the Person Designated in each area to ensure that these actions are completed within the agreed timeframes, documented appropriately, and that the completion date is communicated to the NJRO Quality Management team. Where agreed actions cannot be completed, this should be discussed with the NJRO Quality Management team, and a suitable course of action agreed.

6.5. Adverse Event Closure

Once the NJRO Quality Management team is satisfied that all CAPAs have been implemented, and no further action is required, the adverse event will be marked as closed on the adverse event log. The final section of the CAPA table attached to the Adverse event report should be signed off to indicate this status. All relevant parties will be informed by e-mail.

The signed original Adverse Event Report will be retained for up to 10 years.

7. References

www.hta.gov.uk

- Code of Practice A – Guiding Principles and the fundamental principles of consent
- Code of Practice E: Research