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Approval History				
Version 1.0	Name	Role	Signature	Date
Written By:	Matthew Purcell	Director of H&S		02.03.2020
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Version 2.0	Name	Role	Signature	Date
Revised by:	Linda McLatchie	Hub PD (acting)		03.06.2023
RIGO approval:	Gill Fairburn	Interim Director R&I Services		26.06.2023
DI approval:	Paul Townsend	DI		19.06.2023

1. INTRODUCTION

It is important that organisations conducting human tissue research have systems in place to ensure all adverse events relating to the use of human tissue are investigated promptly. This includes ensuring effective corrective and preventative actions are taken where necessary and improvements in practice are made. The Human Tissue Authority states that *all establishments licensed by the HTA are required to have an internal system for reporting adverse events and, where necessary, instigating an investigation or root cause analyses*.

This Standard Operating Procedure (SOP) outlines the process of identifying, reporting, logging, addressing and monitoring Adverse Events/Incidents (AE/I) associated with the acquisition, storage, use and disposal of human tissues for research purposes. Examples of AE/I include specimen loss, missing or incorrect documentation, security breach, abnormalities in storage temperature readings and inappropriate disposal.

2. SCOPE

This SOP is applicable to all AE/I in relation to human tissue research being conducted under the auspices of the University of Surrey whether on or off site. It details the reporting mechanism for an AE/I, the responsibilities for reporting and taking corrective and preventative actions to demonstrate closure, and the process for assuring its requirements continue to operate effectively.

3. RESPONSIBILITIES

3.1 The Designated individual (DI) has *a legal duty to ensure that statutory and regulatory requirements are met. They are responsible for supervising licensed activities and ensuring suitable practices are taking place*. This includes having overall responsibility for the implementation of an appropriate AE/I reporting process in accordance with the University's obligations under its HTA Research Licence.

3.2. The Persons designate (PD) *assist the DI in ensuring compliance with HTA standards.* There is a PD for each of the areas; Stag Hill (Hub PD and FEPS PD), Leggett, VSM, VSP and Surrey CRB. They are responsible for ensuring that immediate preventative actions are taken following the detection of an incident to minimise any further harm to tissue samples, the donors of samples and studies. They are also responsible for assisting in the completion of the AE/I form and sending it to RIGO. They should assist in any investigation that is necessary to identify the root cause of any AE/I and monitor the completion of actions. The Hub PD is additionally responsible for notifying and keeping the DI informed in a timely manner determined by the severity of the AE/I.

3.3. The Human Tissue Research Operations Group (HTROG) is the governing body who will on behalf of the DI, review the ongoing effectiveness and implementation of the AE/I reporting process and ensure action is taken to address any University-wide emerging AE/I trends, including any system failures.

3.4. The principal (or lead) investigator (PI) is responsible for ensuring that they follow the guidance in all SOPs and their studies are compliant. Where a problem is identified they, are responsible for ensuring their team are familiar with the reporting requirements set out in this SOP and ensuring the AE/I is reported accurately and that any corrective and/or preventative actions resulting from the investigation are completed. For student projects, the PI responsibility falls on their supervisor.

3.5. Research Integrity and Governance Office (RIGO) is responsible for checking AE/I for any repeating patterns that suggest that further action or training may be needed for a particular group of individuals or more generally. They are responsible for coordinating the review and sign off for the AE/I and assisting in the indentation of the root cause and monitoring the completion of actions. Where necessary, RIGO will notify the ethics committee which originally provided the favourable ethical opinion.

3.6. All staff, students and visitors who collect, store, use or dispose of human tissue for research being conducted under the auspices of the University must ensure they adhere to this SOP. They must report the AE/I to the PD for their area immediately and complete an initial AE/I report form, assist with any investigation, and comply with any identified corrective and preventative action(s).

4. PROCESS

4.1. Definitions:

4.1.1. An adverse event is any event that:

- caused harm or had the potential to cause harm to staff or visitors.
- Led to or had the potential to lead to a breach of security of the premises and the contents contained therein.
- Caused harm or had the potential to cause harm to stored human tissue (including loss)
- Gave rise to an internal inquiry.

4.1.2. An incident is any untoward event or sequence of events:

- That caused or had the potential to cause damage, harm or have a direct negative impact to an organisation's business, security, reputation, facilities, personnel, safety, health and environment.
- Where an important policy, procedure or practice was not followed by staff leading to detrimental or the potential detriment of the above.

Category	Examples of adverse events and incidents:
Consent	• Human tissue removed from patient/participant without appropriate consent • Human tissue stored without appropriate consent • Human tissue acquired, stored, used or disposed of without appropriate consent • Staff member seeking consent is not appropriately trained • Human tissue used for research project without ethical approval
Governance and quality	• Conduct of non-licenced activities • Wrong version of SOP in use/failure of change control mechanisms • Breach of data protection/confidentiality (e.g., sample with identifiers) • Research material transferred without a MTA or equivalent
Sample taking	• Wrong type of specimen • Incorrectly labelled specimen • Specimen from wrong patient/participant • Specimen in wrong format
Tracking	• Labelling error • No record of stored sample on recording system • Sample logged on recording system 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
Transport	• 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.

Table 1: Illustration of some of the AE/I that could occur. Please note that this list, only gives some examples in each category and is not an exhaustive list. If in doubt about whether an AE/I has occurred, the area PD should be consulted.

4.2 Reporting and investigation of AE/I involving human tissue samples held under the HTA licence. Any AE/I that occurs that involves samples being stored under the authority of the HTA licence should be dealt with and reported following the guidance and timelines in the table below.

Step	Person responsible	Action	Time frame
1	Person observing the AE/I	Take any immediate preventative action required, such as transfer of samples to alternative location or make safe spillages.	ASAP and all within the same day as AE/I being observed.
2	Person observing the AE/I	Inform the lab manager and PD for that area	
3	Area lab manager/PD	Take any further action required to prevent risk to the samples, other samples, donor of samples or to the study such as placing samples in quarantine or moving additional samples.	
4	Lab manager/PD	When person reporting the AE/I is not the PI the PI should be informed of the AE/I and any action taken. In cases of equipment failure PIs of all affected studies should be informed	
5	Person identifying the AE/I	Complete an initial AE/I report using UOS_RIGO_template_013 Adverse Event/incident (AE/I) Report form.	Next working day after AE/I was observed.
6	Person identifying the AE/I	Send initial AE/I report form to area PD and PI, if not the PI, to check/discuss details.	
7	Area PD	Notify the hub PD and send a copy of the initial AE/I	
8	Hub PD	Review the form, check that all preventative action that is needed has been taken and suggest initial severity grading (see appendix 1). Send AE/I to RIGO integrity and to DI if categorised as Major or Catastrophic.	

9	RIGO integrity	Review report, check the initial category and contact the Hub PD ASAP if the category needs to be increased to Major or Catastrophic.	Next working day
10	RIGO, PD, PI, lab manager and anyone else involved	Investigate the incident further to identify what factors lead to it happening and what actions are needed, to provide more information and to reduce the risk of AE/I happening again	Within 5 working days of initial report
11	Area PD	Add to AE/I with more information and suggested actions and inform local staff of any immediate corrective and preventative actions (CAPA). Send follow-up AE/I to hub PD.	
12	Hub PD	Add any additional actions to the follow-up AE/I, suggest any changes to the category and send to RIGO integrity. Send an update to the DI if originally graded as major or catastrophic or now is.	
13	DI	If the follow-up AE/I identifies the severity as catastrophic or major and the DI thinks that a CAPA plan is required, they should set up a preliminary meeting with a senior member of RIGO staff and other senior managers and appropriate personal, to agree the CAPA plan required, contacting external bodies (e.g., HTA) for advice as appropriate.	Within 5 working days of receiving the follow-up AE/I
14	RIGO, PD, PI, lab managers and anyone else involved	Where the category is moderate or lower any further investigation or actions required should be assigned by RIGO or the PDs.	
15	Hub PD	Update the AE/I with any additional information and suggest final severity category. Send final report to RIGO and the DI and report incident to any other PDS not already involved.	Once all information has been collected

16	RIGO integrity	Log AE/I report on the University's Human Tissue Governance SharePoint site and check final categorisation. Report at the next Human Tissue Research Operations group meeting.	
17	PI, PD, research staff, Lab managers etc.	Complete any actions assigned to them	Within the agreed deadlines set out in the CAPA plan
18	PI to action any decisions made by, DI, RIGO, PD. Lab managers to control sample access.	All samples placed in quarantine should remain in quarantine until the AE/I has been fully investigated and resolved and actions completed. In cases where samples cannot be kept, they should be destroyed or returned to the sender within 10 days of this being determined.	Any actions to return or destroy samples should be carried out within 10 days of decision being taken

NB:

1) In cases where an AE/I is detected a significant time after it occurred, such as issues found during auditing, the AE/I initial report should be submitted and investigated as above but the exact time frame may be relaxed unless the AE/I is classified as major or catastrophic.

2) Where the person listed as responsible for an action is unavailable such as due to leave or sickness, for longer than it is appropriate to wait, the person responsible for the previous step should follow through the required action to enable the processes to proceed in a timely way.

4.3. Reporting and investigation of AE/I involving human tissue samples with NHS rec or other REC approval. Any adverse event or incident that occurs that involves human tissue samples being stored which have research ethics committee approval should be reported as detailed below.

4.3.1. The person identifying the AE/I should take any immediate preventative action required to make any samples or equipment involved safe and minimise further damage and then report the AE/I immediately to the study PI and local lab manager.

4.3.2. The study PI should complete an initial AE/I report, using (UOS_RIGO_template_013 Adverse Event/incident (AE/I) Report form) and send it to RIGO integrity (integrity@surrey.ac.uk) as soon as possible.

4.3.3. RIGO will review the AE/I and advise the PI if any actions are required. RIGO will contact the hub PD if any of these actions are lab-based to help assist with these

and also in cases where the PI also has samples held under the HTA licence or the incident involves storage equipment. The hub PD will then contact the lab manager for the area involved and together with RIGO, will monitor the completion of these tasks. Where necessary, RIGO will notify the ethics committee which originally provided the favourable ethical opinion.

4.3.4. RIGO will keep a record of all AE/I and keep members of the Human Tissue Research Operations Group (HTROG), and Research Integrity and Governance Committee (RIGC) informed of any major or catastrophic AE/I that occur involving samples with REC approval.

6. ASSOCIATED DOCUMENTS

UOS_RIGO_template_013 Adverse Event/Incident (AE/I) Report Form
UOS_HT_SOP_03 Training requirements for using human tissue

7. REFERENCES

HTA Code of Practice and Standards: Code E, Research

7. TRAINING

Before commencing any work with human tissue samples anyone wishing to do so must have completed all the training detailed in UOS_HT_SOP_03, Training requirements for using human tissue.

8. USEFUL ABBREVIATIONS

HTA – Human tissue authority
HRA – Human Research Authority
HT Act – Human Tissue Act
LH - Licence holder
DI- Designated individual
RIGO – Research Integrity and Governance Office
HTROG – Human Tissue Research Operations Group
PD- Person Designate
SOP-Standard Operating procedure
AE/I - Adverse event or incident
GCP – Good Clinical practice
MTA – Material Transfer Agreement
REC – Research Ethics Committee
UEC- University Ethics Committee
CAPA- Corrective Actions and Preventative Actions

9. REVISION HISTORY

Version number	Revision details	Author	Date
1	New document (UOS_HTA_SOP_013)	Matthew Purcell	02/03/2020
2	Major revision including new number (UOS_HT_SOP_11)	Linda McLatchie	03.06.2023

Appendix 1 – Grading of Adverse Events/Incidents for human tissue research activities

Severity Level	Description of Adverse Event / Incident (not exhaustive list)
5 Catastrophic	▪ Loss of unique human tissue that impacts on a study or potential future studies ▪ Loss of participant identification records in public area or during transportation
4 Major	▪ Loss of human tissue not classed as unique ▪ Human tissue removed from a participant, stored or used without appropriate consent ▪ Staff member seeking consent or working with human tissue who has not completed the approved training. ▪ Human tissue used for a research study which has not been approved by the appropriate Research Ethics Committee ▪ Breach of Data protection/confidentiality ▪ Incorrect type of specimen acquired or from wrong participant, specimen incorrectly labelled, specimen in wrong format ▪ Freezer/Nitrogen back-up and alarm failure resulting in destruction of material ▪ Unauthorised removal of material from a storage facility ▪ Human tissue placed with non-clinical or animal waste for disposal ▪ Quality of human tissue significantly compromised during transportation
3 Moderate	▪ Human tissue transported to or from University of Surrey without appropriate contract/material transfer agreement (MTA) in place ▪ Labelling error that can be accurately rectified ▪ Not using a tracking system to record material acquisition, storage, use and disposal ▪ Inappropriate transport of specimens
2 Minor	▪ Incorrect version of policy or SOP in use ▪ Not registering new SOPs or updating existing ones on the RIGO website
1 Insignificant	• Incident occurred which resulted in no compromise of human tissue
0 Near miss	• AE/I could have happened if intervention had not been made