Human Samples in Research Standard Operating Procedure 5
Adverse Events

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Revision Chronology:	Effective date:	Reason for change:
HSR SOP 5_V1.02	13 December 2010	Clarification of University policy – QMS applies to all human samples. Creation of the role of Administrative Officer, Deputy DI and changes to the role of PD. Reorganisation of Biological Sciences to form the School of Life Sciences.
HSR SOP 5_V1.03	10th January 2012	Changes in staff, room numbers and external links.
HSR SOP 5_V1.04	25 February 2015	Changes to University governance structures relating to human samples.
HSR SOP 5_V2.0	14 July 2023	Various updates including changes made for clarity, accuracy and readability, removed sections duplicated in each SOP (to be included in Quality Manual), added reference to University's agreed three-tier 'risk-based' approach, links to HTA guidance updated as appropriate.
HSR SOP 5_V2.1	24 February 2024	Links updated

Adverse Events

1. Purpose and scope

The purpose of this Standard Operating Procedure (SOP) is to ensure that all staff and students understand the requirements and procedures for recognising, managing and reporting any adverse event or incident related to human samples for research, covered by the Human Tissue Act 2004 (HT Act), the Human Tissue Authority's (HTA) Codes of Practice, the University's HTA licence for research and the University's Quality Management System for the governance, storage, and disposal of human samples for research.

2. Background

This SOP forms part of the University's Human Samples in Research Quality Management System (QMS). All research involving human samples at the University of Warwick must comply with this Quality Management System.

The University requires that all human samples defined as relevant material by the HTA and held at the University for Research shall meet the standards of quality management set out in its standard operating procedures. For the avoidance of doubt, this includes any cellular human material, regardless of whether it has current REC approval, unless it is a cell line that has been passaged at least three times. A risk-based approach will be applied.

This SOP has been produced in accordance with the HT Act which came in to force on 1 September 2006, and should be read in conjunction with the HTA's *Codes of Practice*, available at: https://www.hta.gov.uk/guidance-professionals/codes-practice-standards-and-legislation

3. Definitions

In keeping with its HTA Research Licence, the University has an internal system for reporting adverse events and, where necessary, instigating an investigation or root cause analysis.

The definition of an adverse event for the purposes of this SOP is as follows:

Any event or incident that may, or has the potential to, result in the theft, damage or loss of human samples or may compromise the University's compliance with its licensing obligations under the HTA, or the good governance and output of research using human samples.

Staff working under the HTA Research Licence must understand what is meant by an adverse event and the procedure to follow when such an event occurs.

4. Procedure

4.1 Responsibilities

The Registrar (as the Licence Holder's Representative) and the Designated Individual (DI) are responsible for ensuring that appropriate procedures are in place, and that staff and students involved in research using human samples are appropriately trained. The DI is responsible for maintaining a log of adverse events involving human samples. In the event of incidents, the DI may investigate

further, with the support of other staff as necessary. The DI is responsible for reporting the adverse event or incident to the Licence Holder and/or the HTA, if necessary.

The Principal Investigator (PI) is custodian of the samples and is responsible for reporting any adverse events or incidents to the DI. They are responsible for managing adverse events and incidents within their laboratory and team, assisting with investigation if necessary and ensuring that learning opportunities are managed without blame and for maximum benefit.

Individual researchers are responsible for being alert to the possibility of adverse events and incidents occurring and for drawing them to the attention of their Principal Investigator or Person Designated.

Persons Designated (PD) are responsible for helping to manage adverse events and incidents, and for notifying the DI if necessary.

Heads of Department are responsible for ensuring that members of their department comply with the SOPs for working with human material.

The Human Samples Steering Group (HSSG) is responsible for approving all SOPs. Substantial amendments to existing SOPs, the creation of new SOPs and changes to the Quality Management System, will require approval by the HSSG.

The University has delegated responsibility for the regular review of HTA SOPs to the Human Tissue Act Designated Individual (HTA DI) and Research Governance Team in Research & Impact Services (R&IS).

4.3 How?

4.3.1 Identifying an adverse event

All staff and students working with human samples should be vigilant and alert to the actual, or potential for, theft, damage or loss of the material, as it occurs or once it has occurred.

All staff and students are encouraged to identify any event they believe may compromise the University's compliance with the licensing obligations under the HT Act or the good governance and output of their research using human samples. Examples of adverse events are listed below as a guide to the types of events that might require a report, but this is not an exhaustive list.

Further advice on the identification or handling of an adverse event may be sought from the PD or the DI. The DI will seek advice directly from the HTA as appropriate. Examples of adverse events include:

Consent and ethical approval

- Human tissue collected, stored or used without appropriate consent;
- Human tissue collected, stored or used without appropriate ethical approval.

Governance and quality

- Wrong version of SOP in use;
- Breach of Data protection/confidentiality of individual donors;
- Material transferred without appropriate authorisation (Material Transfer Agreement/ Import Authorisation Form/ Export Authorisation Form.

Import of samples

- Samples received without relevant approval from the DI;
- Incorrect sample received;
- Unlabelled or unidentifiable sample received;
- Sample in inappropriate or unusable condition;
- Sample packaging damaged in transit and samples compromised.

Sample tracking

- Sample labelling error or missing label;
- Information about stored material not updated on Sample Register;
- Discrepancy between storage location and record on Sample Register;
- Incomplete audit trail resulting in inability to trace a sample.
- Missing sample.

Premises, equipment and facilities

- Cold storage/freezer breakdown with alarm failure that is caught in time – near miss;
- Cold storage/freezer breakdown with alarm failure that is **not** caught in time - sample compromised;
- Unauthorised access to storage facilities/breach of security;
- Human samples stored in inappropriate storage containers and/or inappropriate conditions.
- Nitrogen tanks not topped up sufficiently to maintain tissue quality.

Disposal

- Human samples disposed of with general clinical waste or general waste;
- Record of disposal of samples not updated on Sample Register;
- Incorrect or failure to label human sample waste.

Export of samples

- Samples transferred without appropriate authorisation (outgoing MTA/Export Authorisation Form);
- Samples lost during transportation;
- Sample quality compromised during transportation.

4.3.2 Storage equipment failure

All laboratories have a management plan in case of equipment failure. Emergency -80°C freezers at the hub and satellite sites are unlocked and labelled in line with the protocol for human sample storage unit labelling (see HSR SOP 4 Storage).

Freezers used to store human samples at -80°C and at -40°C have independent alarm systems provided by Britannia Alarms (separate from in-built alarms). If an alarm is triggered by the Britannia system, a text detailing the site and which freezer or room alarm has been activated (e.g. CSRL ALARM ON FREEZER No. 6) is sent to members of the technical team.

Upon receiving an emergency alert text, members of the technical team will consult with each other to determine who will attend the incident. The texts continue to be sent until the fault is resolved and the alarms are deactivated at source. On arrival at the site, the member of the technical team will assess the conditions, and a decision on the need to re-locate the samples, for example, to an emergency freezer will be taken. If appropriate, the samples will be moved to the emergency freezer which will be re-labelled to indicate that it contains material of human origin. The member of the technical team attending the incident will inform the DI by telephone or email within 24 hours of the action taken.

Should there be an emergency situation at the hub or satellite site that renders the storage units and/or the premises unusable then the human samples will be transferred to the other site until the original site is functional.

4.3.3 Power failure

In the event of an unplanned loss of power, all freezers will be connected to an emergency back-up generator as quickly as possible.

At the satellite site (Gibbet Hill and Main Campus) upon discovering a power failure, a call should be logged through to the Estates Helpdesk (Extension 22567). Estates will mobilise electricians as a matter of urgency. If the team is not able to reconnect the power supply (for example, in the event of a failure of the national grid) Estates will mobilise a generator to supply energy to the freezer rooms.

At the Hub site (CSRL), the emergency generators are expected to start automatically in the event of a power cut. If this does not happen, call the PFI Helpdesk on extension 25555. Inform them of the issue, state it is urgent, and get a reference number. Ask for an estimate of the time for someone to attend. Be prepared to keep chasing the call because this helpdesk covers the entire hospital site. Notify the PD and the DI of the incident and the reference number. They will also make contact with the helpdesk to assist its swift resolution.

During a power failure, open freezer doors as little as possible to conserve the temperature of the freezer/fridge/incubator.

4.3.4 Disposal of samples following an adverse event

In the event of catastrophic failure of a freezer or storage facility, the DI will arrange the safe disposal of unusable samples (in line with HSR SOP 6 Disposal).

If samples are moved to an emergency location, at the earliest opportunity, and within 24 hours of the incident, the DI will inform the Lead Investigator of the new location of the samples.

The Lead Investigator is responsible for updating the record on the Sample Register, in accordance with HSR SOP 4 Storage. Updating of the Sample Register must be completed at the earliest opportunity and within one week of the incident.

4.3.5 Reporting an adverse event

All adverse events or incidents involving human samples stored or used for research must be reported to the DI immediately when they occur or they are found to have occurred.

Any event or incident that has caused the loss of human samples or damage to human samples must be reported to the DI. "Near miss" events should also be reported where there was the potential for loss or damage.

A Human Sample Adverse Event/Incident Report (see Appendix 1) must be completed and submitted to the DI as soon as possible, and within 24 hours of the Lead Investigator being informed of the incident. The Lead Investigator is responsible for ensuring this form is completed and submitted to the DI. The DI will log the adverse event.

4.3.6 Investigating an adverse event

All adverse events and incidents involving human samples reported will be investigated by the DI, with assistance from PDs, PIs and others as appropriate. The checklist used to support the investigation is shown in Appendix 2. The investigation will be reported by the DI to the Human Samples Steering Group and the DI will inform the relevant Head of Department. The investigation will be reported to the GMBSC and HTA, as appropriate.

5. Training

All those involved in research involving human samples are required to read this SOP and to understand how its requirements relate to their research. Your acknowledgement of the SOP will be recorded in the Q-Pulse electronic quality management system and will form part of your Personal Training Portfolio (PTP), explained in HSR SOP 7 Training. Individuals will be expected to recognise an adverse event and understand the requirements for reporting it.

6. Advice and guidance

Further advice on recognising and reporting adverse events and the provisions of this SOP may be sought from the DI. The DI may seek advice directly from the HTA when appropriate.

7. Monitoring and audit

Monitoring of the effectiveness of the implementation of this SOP will be undertaken by the DI and/or others nominated by the DI. In addition, audits may be undertaken by the DI, the University's Internal Audit Service or the HTA, in accordance with HSR SOP 8 Audit.

List of Abbreviations

HTA	Human Tissue Authority
HT Act	Human Tissue Act 2004
DI	Designated Individual
HSSG	Human Samples Steering Group
PD	Persons Designated
PI	Principal Investigator
R&IS	Research & Impact Services
SOP	Standard Operating Procedure

Templates/Associated Documents

Appendix 1: Human Sample Adverse Event/Incident Report
Appendix 2: Investigation Checklist

Appendix 1

University of Warwick

Human Sample Adverse Event/Incident Report

Title:	
Surname:	
Forename:	
Telephone contact number:	
Email:	
Job title:	
Department:	

Adverse Event/Incident details

Event/ Incident Date:		**Time of Event/ Incident:**	
Location (Please provide specific details):			

Description of Adverse Event/Incident: Please give specific detail

Did the event / incident result in loss or damage to human material (delete as appropriate)	**Yes**	**No (near miss)**

What action has been taken:

Name of person completing the Adverse Event/Incident Form:……

Please Print

Date form completed:……

Name of HTA Designated Individual:……

Has the HTA Designated Individual been notified already? Yes / No

Please forward a copy of this form to the DI at hta@warwick.ac.uk

For office use only:

Adverse event / Incident number:……

Appendix 2

Investigation Checklist

SOP	Is there a SOP to cover the procedure?	Yes/No
	If yes:	
	Is it adequate?	
	Does it need to be revised?	
	Did the individual know about and follow the SOP?	
Training	Was the individual appropriately trained?	Yes/No
	If not, why not?	
Equipment/ facilities	Was the equipment/facilities/security fit for purpose? If not, why not?	Yes/No
Previous occurrence	Have similar incidents happened before? If yes, give details	Yes/No
Immediate Corrective Action	Was any immediate corrective action performed? If yes, give details	Yes/No
Preventative Action	Has any preventive action been performed or planned? If yes, give details	Yes/No
Review incident	Has the incident (including corrective/preventative actions) been reviewed at the HSSG? Specify date:	Yes/No
HTA Notification	Is HTA Notification required? If yes, state date completed:	Yes/No
Follow up	Is the action plan complete? Date of closure:	Yes/No