

Human Tissue Handling – Health and Safety

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Human Tissues in the Laboratory	1
General guidelines	4
Risk assessments.....	5
Definitions.....	5
General.....	6
Performing a risk assessment.....	7
Acquiring Human Samples	8
Acquiring consent for use of human tissue samples	10
Handling Human Tissue Samples	14
Designated laboratories.....	14
Techniques	15
Training requirements for human tissue users	15
Protective Equipment.....	16
Generic	17
Personal.....	18
Environmental contamination control.....	19
Safety cabinets	20
Leakages	22
Leaking Sample Recovery Protocol.....	23
Breakages	24
Major Spillages	25
Small Spillages.....	25
Labelling human tissue samples	26
Logging the storage of human tissue samples	Error! Bookmark not defined.
Packaging and transporting Human Tissue Samples	28
Between laboratories.....	Error! Bookmark not defined.
Local transfer	29
Import and export.....	Error! Bookmark not defined.
Record keeping	33
Disposal of Human Tissue Samples and Associated Materials and Decontamination	
Procedures.....	34
Disposal of Associated Materials.....	36
Equipment decontamination	38
Centrifuge Decontamination.....	38
Class I Protective Cabinet Decontamination	39
Class II Protective Cabinet Decontamination	40
Record Management	Error! Bookmark not defined.
Accident Reporting	44
Adverse Event Reporting.....	44
Complaints Policy	45
Governance Policy	48
Staff responsible for implementing procedures on Human Tissue Samples	49
The ISTM Human Tissue Committee reference and membership.	50
Associated Documents.....	52
Risk Assessment form for activities involving biological agents	53

COSHH assessment: Institute of Science & Technology in Medicine..... 66
Keele University Independent Peer Review Application Form... **Error! Bookmark not defined.**

Human Tissues in the Laboratory

General guidelines

1. Person handling biohazardous material should be immunised against Hepatitis B and their response to the immunisation checked. The accuracy of this information must be updated at least annually by the group heads and recorded centrally (see Jeanette Forrester).
2. No person who has not been trained by a senior staff member (supervisor or delegated deputy), and authorised to do so, can handle human specimens.
3. All persons proposing to handle such specimens must first be thoroughly familiar with the contents of this protocol and other associated procedures referred to herein.
4. Full risk assessment must be performed on all standard operating procedures using human material prior to use by any personnel (including senior staff). Subsequently, the relevant risk assessments must be read and understood (with signed confirmation that this has been done) by all staff prior to performing the procedure.
5. All personnel handling human material must first have read and signed that they have understood the laboratory safety manual.
6. Processing of samples must be performed in dedicated areas (see Page 17).
7. Only designated area are to be used for the storage of samples of human material (see Page 17).
8. CJD patient samples- contact head of dept, or Consultant Microbiologist (Dr George Orendi) immediately for advice before handling.
9. Facilities for the handling of samples with a high probability of infection risk are not available within the Keele laboratories.
10. For activities relating to materials covered under the Human Tissue Act a Biological Risk Assessment should be performed first followed by a detailed breakdown of the associated activities/process in the generic ISTM COSHH form. The biological risk assessment form and all associated Appendices are located on Page 52 –Page 64. The ISTM COSHH form is located on Page 65 – Page 66.

Definitions

‘Human material’, in the context of this document, includes blood samples, urine, tissue samples, and any other material of human origin (e.g. cerebrospinal and other fluids).

Risk assessments

Definitions

- 1) A risk assessment (RA) describes the steps taken to identify a hazard and a measure of the probability of risk occurring due to that hazard.
- 2) Risk is the chance of injury, damage or loss.
- 3) A hazard is something that is, or has the potential to be, dangerous. These can be;
 - a) Physical
 - b) Chemical
 - c) Biological
- 4) Risk assessments should be suitable and sufficient such that appropriate levels of depth, control and monitoring are applied.

General

- 1) A RA must be generated in advance for each new protocol implicated in the handling of human tissue.
- 2) A RA should be undertaken for each staff member identifying specific risk areas which they are exposed to and what measures can be applied to minimize that risk.
- 3) The individual RA should identify
 - a) Work which cannot be undertaken without direct supervision by a person of responsibility
 - b) Work which requires prior instruction on safe working by a person of responsibility before it can be started
 - c) Work which presents little hazard and can be safely carried out without prior instruction.
- 4) This should be performed;
 - a) When that person starts work.
 - b) Minimally on an annual basis.
- 5) Included in the RA should be the relative dangers associated with handling;
 - a) Biological specimens
 - b) Infectious agents
 - c) Chemicals and solvents
 - d) Equipment
- 6) Where the protocol involves handling human tissue has the risk of patient identification been eliminated?
- 7) In all instances it is the responsibility of the human tissue handler or experimental practitioner to identify and minimize the risk exposure.
- 8) An RA should only be performed by a practitioner who has sufficient knowledge of;
 - a) Hazard Identity.
 - a. Physical
 - b. Chemical
 - c. Biological
 - d. Equipment
 - b) Associated hazard safety procedures.
 - c) Laboratory safety features.
 - d) Knowledge of governing regulations
- 9) The category into which each operation is placed will be made by the person of responsibility with due attention given to the likelihood that the operation can be carried out safely with the defined amount of supervision, not on whether time is available to give that supervision.
- 10) All active RAs should be reviewed , minimally, annually and/or whenever a modification occurs to the laboratory which may have an impact on the RA;
 - a) New employee.
 - b) New reagent.
 - c) New equipment.
- 11) Where a hazard cannot be reasonably controlled, the risk must be transferred to those competent to deal with it e.g. a supervisor, responsible person, specialist contractor.

Performing a risk assessment

- 1) Evaluate laboratory features
 - a) Physical facility
 - i) Air Flow
 - ii) Access
 - iii) Structural composition.
 - b) Containment equipment
 - i) Safety cabinets
 - ii) Fume hoods
 - c) Personnel
 - i) Experience
 - ii) Training
 - iii) Immunization
 - iv) Disability
- 2) Evaluate procedural features.
 - a) Biological/Chemical agent
 - i) Pathogenicity
 - ii) Mode of transmission
 - (1) parenteral
 - (2) blood
 - (3) ingestion
 - iii) Information available e.g MSDS
- 3) Procedures performed
 - i) Aerosol generating
 - ii) Use of syringes and needles
 - iii) Extreme temperatures
 - iv) Sterile technique
- 4) Assess features and categorize risk
 - a) Do any features carry with them a risk of;
 - (1) Death or cause permanent disability
 - (2) Long-term illness or serious injury
 - (3) Medical attention and several days off work
 - (4) First aid needed
 - b) Judge the likelihood of it happening
 - i) High
 - ii) Medium
 - iii) Low
 - iv) Very low
- 5) Maximize efforts to minimize risk to Low/Very Low likelihoods in all instances.

Acquiring Human Samples

The procedure for acquiring human tissue samples is detailed in the HTA-2 Standard operating procedure available on the Keele University Research Governance webpages

1. All self- or internally-funded human tissue research projects involving relevant materials obtained from non-commercial sources should be subject to Independent Peer Review (IPR) prior to application for ethical approvals. If a human tissue project has been funded externally in a process in which peer review has not been obtained as part of the application process, these should also apply for IPR. This can be done by completing the IPR form from the Keele Research Governance Website (Link below). Further guidance can be sought from Nicola Leighton (contact details below)
2. Following successful independent peer review, any study utilising relevant human materials **MUST** receive ethical approval from the Keele Research Ethics Committee (REC) for healthy human tissue, or the NHS REC for NHS-based studies. Section 3 for links to the application forms. For guidance with these applications, please contact the individuals below as appropriate.

<p>Keele University contacts:</p>	<p>University Hospital North Midlands Trust (UHNM) contact:</p>
<p><u><i>For NHS-based studies</i></u></p> <p>Emma Skinner Sponsor QA Manager Directorate of Engagement and Partnerships iC2 Building Keele University ST5 5NH</p> <p>Telephone: 01782 733374 E-mail: e.skinner@keele.ac.uk</p> <p><u><i>For all other research</i></u></p> <p>Nicola Leighton Research Governance Officer Directorate of Engagement and Partnerships iC2 Building Keele University ST5 5NH</p> <p>Telephone: 01782 733306 E-mail: n.leighton@keele.ac.uk</p>	<p><u><i>For NHS-based Studies</i></u></p> <p>Dr Darren Clement Research and Development Manager Honorary Senior Research Fellow – Keele University Research and Development Department Academic Research Unit Courtyard Annexe – C Block Royal Stoke University Hospital University Hospitals of North Midlands NHS Trust Newcastle Road, Staffordshire, ST4 6QG Telephone: 01782 675379 Email (PA): louise.barlow@uhns.nhs.uk</p>

- 3.** If material is being obtained from commercial sources, then no ethical approvals or IPR are required. However a clear ethical statement should be obtained confirming that the materials were sourced using methods that meet the regulatory requirements of the HTA.
- 4.** Any work to be carried out using human embryonic stem cells (hESC) must be approved by the UK Stem Cell Bank (UKSCB). All hESC should be sourced from the UKSCB. If cells are not sourced from the UKSCB then Approval to Import should be sought from the UKSCB.
- 5.** Acquisition of human tissue samples from non-commercial sources external to Keele University of UHNM must be conducted under a material transfer agreement. These must be developed in association with the Directorate of Engagement & Partnerships at Keele University. (<https://www.keele.ac.uk/admin/directorateofengagementpartnerships/>). Staff should contact Clare Stevenson to discuss the requirements of their research project (Clare Stevenson, Academic Legal Services Advisor, 01782-734491; c.stevenson@keele.ac.uk)
- 6.** Where it is necessary to have Material Use Licenses (MUL) or Memoranda of Understanding (MOU) or other agreements, these must also be developed in association with the Directorate of Engagement & Partnerships at Keele University as outlined in **2.6** above.
- 7.** A copy of any agreements held with suppliers should be held by the local research team, and a copy should be provided to the human tissue officer for their records.
- 8.** Prior to acquisition of human tissue samples, the principal investigator should complete and submit the following documents to the local human tissue officer (a.g.s.harper@keele.ac.uk (GHRC) or d.p.tonge@keele.ac.uk (Huxley)):
 - HTA-31: Human Tissue Risk Assessment
 - HTA-41: Standard Operating Procedure for human tissue projects
 - HTA-42: Human Tissue Users register (*for all members of research team*)
 - HTA-43: Human Tissue Handling logbook (*for all members of research team*)Copies of all of these forms and their associate SOPs are available on the Keele University Research Governance website
- 9.** All human tissue samples used for research must have been acquired with the informed written consent of the donor (or their nominated representative) using the procedures detailed in the HTA-37 SOP. Where consent is being sought directly by the investigators or on behalf of the investigators signed consent forms must be obtained for all samples, these must be stored securely by the Chief Investigator of the study in a locked, metal filing cabinet, or on a password protected device. Completed consent forms must be made available for inspection upon request by any Secretariat-approved internal or external auditing body.
- 10.** Tissue samples obtained from non-hospital sources such as licensed tissue banks will have established consent procedures. If using tissues obtained from a tissue bank, LREC consent documentation need not be held by the Chief Investigator, although confirmation of its appropriate acquisition by the supplier should be established via the MTA.

Acquiring consent for use of human tissue samples

The Human Tissue Act places the appropriate acquisition of consent of human tissue as a central tenet of all human tissue research. Removing, storing or using human tissue for a scheduled purpose (such as research) without appropriate consent is an offense under the Human Tissue Act (2004). For consent to be appropriate it must have been given by the correct person as defined by the HTA codes of practice on consent (see below). This will often be the donor themselves. However, in the case of deceased donors, or in children or adults lacking the capacity to provide consent themselves, this may be a nominated representative, or those with a qualifying relationship to the donor. Investigators must ensure that consent is obtained from appropriate individuals prior to acquiring, storing or using any human tissue samples.

Appropriate consent must also be *valid*. For consent to be valid it must be provided *voluntarily, by an appropriately informed individual, who has capacity to provide consent*. This process is a sensitive and difficult task and therefore must be performed by an appropriately trained individual.

The *HTA-37 Standard Operating Procedure on acquiring consent* details the procedures that must be followed to ensure that appropriate, valid consent has been obtained for use of human tissue for research purposes (see Research Governance Webpage).

1. All of the procedures that individual research projects use to obtain consent from their participants should be subject to ethical approval from either an NHS Research Ethics Committee (NHS REC) or one of Keele University's Ethical Review Panels (ERPs). All human tissues must be obtained whilst following the guidelines outlined in the University Hospital of North Staffordshire document Policy No. (C43) Policy and Procedures for Obtaining Consent (including the application of the Mental Capacity Act 2005).
2. For human tissue samples that are acquired from sources external to the university, the researcher should seek assurances that appropriate procedures are being used to obtain consent and these have been subjected to scrutiny by an ethical review panel. For non-commercial human tissues, these assurances should be formally documented in a material transfer agreement (MTA), and Keele-based researchers should also seek to obtain documentation of the ethical approval, consent form and information sheets used in the research project. For commercially-sourced tissues, a statement that written informed consent was received should be obtained from the supplier and recorded on the HTA-8 or HTA-9 logbooks.
3. Human tissue projects involving transportation of anonymised human tissue samples obtained at Keele to research groups external to the university should use a MTA to provide formal assurance on the appropriate acquisition of consent for use of the research tissue. The MTA should detail what the donors (or their representatives) have consented for the storage, use and disposal of the tissue sample. Evidence of appropriate

ethical approvals and example consent forms and project information sheets should also be provided to the institution receiving the tissue.

4. Individuals who are being asked to provide consent for the use of a human tissue sample must not be approached about taking part in research until all required ethical and other required governance approvals have been granted.

5. All subsequent stages of the consenting process must be performed by a member of the research team who is fully informed of all aspects of the study (including acquisition, storage, use and disposal of the tissue) and is appropriately trained in the taking of informed consent.

6. The requisite training for an individual who wishes to take informed consent will be the reading of this SOP, the HTA code of practice on consent, the completion of good clinical practice training through the NIHR clinical research network, as well as appropriate experience of having performed this task previously. For individuals who have not taken consent for research purposes previously, the experience component may be gained through documented supervision of consent acquisition of the HTA-43 form. Due to the severity of outcome if consent is not obtained appropriately this activity must be classified as a high-risk activity with a minimum of 10 hours of training and supervision allocated to it. This training and supervision must be completed under the observation of either a PI experienced in taking informed consent for research processes (for studies involving healthy volunteers only), or a clinician or experienced research nurse (for all studies). After completion of this training, the HTA-43 a copy of the logbook should be sent to the the human tissue officer for approval. Once formal written approval has been granted, this individual may perform the acquisition of consent independently.

7. Potential tissue donors who are eligible to participate in the research project (as defined by the inclusion and exclusion criteria) should have the study explained to them (or their representative). Those being asked to provide consent, and their kin, should have an opportunity to ask any questions about the research project.

8. If they are interested in participating they should be provided with a patient information sheet that details all the key information required for the project. For a research project using human tissues, the participant information sheets should provide those providing consent with information on:

- i) The aims of the research project
- ii) Why the donor has been selected for the study
- iii) What the participant will have to do as part of the study
- iv) how the tissue will be taken
- v) the risks and benefits (if any) of these procedures
- vi) how the tissue will be used, stored and disposed of
- vii) the scope of the consent that is being requested (e.g. is consent for specific or generic research purposes)
- vii) the **duration** of the consent that is being requested (how long will the investigators store and use the tissue?).
- viii) the procedure for withdrawing consent for the use of the tissue
- ix) how the information gained from their sample will be used and how the donor's confidentiality will be maintained

x) if the donor will be informed of any findings arising from these studies, and by what processes this will occur.

xi) the contact details for the principal investigator as well as the Designated Individual

xii) the procedure for reporting concerns or complaints about the conduct of the research teams.

9. If the project will involve the analysis of DNA or RNA of the donor's samples, or the xenotransplantation of tissue into animals, these must be *explicitly* stated in the information sheet.

10. This information sheet provided must be accessible for the participant, and therefore may need to be produced in braille, large print or in other languages as required.

11. The project information sheet should be received by the person providing the consent for the use of the tissue as far in advance of the appointment at which written consent will be provided. Unless the study is undertaken in an acute clinical setting where a longer consenting process would be impractical, there should be a minimum of 24 hours delay between the provision of the participant information sheet and the final documentation of consent. This will provide the potential donor with sufficient time to make an informed decision and provide the individual an opportunity to discuss their decision with the research team or other family members or friends.

12. Those being asked to give consent should be aware that they are under no obligation to take part in the study. They should also be made aware that they may withdraw at any point prior to the full use or disposal of the tissue as part of the project without the need to provide a reason for their decision.

13. Those being asked to provide consent should not be influenced by the offer of incentives or the application of duress. It should be made clear to the individual that refusal to give or subsequent withdrawal of consent should have no impact on the treatment and care provided to themselves or their relative by the research team.

14. At the meeting to document consent, the investigator should provide the donor (or their representative) with an opportunity to ask any further questions they have and ensure they have clearly understood how the tissue will be acquired, used, stored and disposed of.

15. The investigator should assure themselves that the donor has the capacity to give consent in line with the Mental Capacity Act (2005) code of practice. If there is any doubt about the individual's capacity to give consent, then consent should not be taken.

16. If the individual providing consent is happy to proceed then they must complete a written consent form with statements confirming that they have i) read and understood the participant information sheet, ii) that they are willing to participate in the study and iii) they are aware they may withdraw consent at any time prior to the tissue being completely used or disposed of as part of the project. The consent form should also provide clear statements about the duration and scope of the consent to be provided. A template of a generic Keele University consent form may be found on the Research Governance webpages.

17. If the project will involve the analysis of DNA or RNA of the donor's samples, or the xenotransplantation of tissue into animals, the consent form must include a section in which the participant *explicitly* confirms their consent to these particular procedures.

18. Human tissues obtained under consent under Keele University ERP or NHS Research Ethics Committee approval must be logged upon entry and Alan Harper (Guy

Hilton Research Centre) or David Furness (Huxley Building) immediately notified and shown the signed consent form. They will provide the relevant HTA-8 or HTA-9 spreadsheet required for logging the acquisition, storage, use and disposal of human tissue samples.

19. Consent forms should be stored securely in accordance with our records management policy (HTA-39). Consent forms should be stored securely in a locked filing cabinet only accessible to members of the research team within a licensed Keele Building. If paper records are removed from secure storage, they should not be left unattended in the absence of a member of the research team. The only exceptions to this would relate to records of donor-related information held by external research partners supplying tissue under the auspices of a material transfer agreement, or those records held by a clinician at the University Hospital of North Midlands Trust. Confidential information relating to the personal information of donors or staff must be stored according to the regulations in Keele University's *Data Protection* and *Confidential Records* policy documents (see references for links)

20. All consent forms must be securely stored in the HTA-licensed premises in which the research is conducted. The only exceptions to this would relate to records of donor-related information held by external research partners supplying tissue under the auspices of a material transfer agreement, or those records held by a clinician at the University Hospital of North Midlands Trust. Written assurances of the storage of these research documents should be obtained and securely stored by the chief investigator.

21. A person may withdraw their consent at any time. If this occurs after formal documentation of consent has been taken, then the consent form should be amended by striking through diagonally with a single red line, and a clear statement of "consent withdrawn" marked at the top with the date of the receipt of the request and the signature of the PI. This form must then be held for auditing purposes. The tissues must be disposed of and recorded on the logging sheet. After this has been done a letter should be sent to the donor confirming the receipt of the request and the actions taken to comply with this request. A copy of this acknowledgement letter should be held alongside the amended consent form.

Handling Human Tissue Samples

Designated laboratories

- 1) Facilities for the handling of samples with a high probability of infection risk are not available within the Keele laboratories.
 - a) These include;
 - i) IV drug users.
 - ii) homosexuals.
 - iii) some tattooed individuals.
 - iv) known positive HIV patients.
 - v) known positive Hepatitis patients.
 - b) If such samples are received, contact a senior staff member who will dispose of the sample.
- 2) The currently designated areas for Handling Human Tissue Samples are;
GHRC - labs 2, 4, 5, 6, 11, and 13 (Medical Research Unit); Genomics lab (Keele Labs); and rooms 1/015 (Clean Utility), 1/016 (Laser Lab), 1/017 (SIFT lab), 1/019 (Incubator Room), 2/001 (Molecular Lab), 2/002 (Histology), 2/006 (Biomaterials), 2/010 (Magnetics), 2/011 (Microwave Lab), 2/014 (CT Scanner), and the Cell Therapy Suites.
Huxley – Rm.152b, Rm.152c, Rm.152d, Rm.155b, Rm.206, Rm.311, Haldane laboratories
Mackay – 120, 122, 123, 125, DT3, DT4
- 3) Tissue samples should not be placed within any office area at any time.
 - a) Tissue samples discovered in any office area will be quarantined and dispatched for incineration.
- 4) Tissue samples should not be placed in any common area at any time.
 - a) Tissue samples discovered in any office area will be quarantined and dispatched for incineration.
- 5) All processes involving handling of human samples must be performed in the designated areas where the surface is impervious to water, resistant to acids, alkalis, solvents and disinfectants, and is easy to clean.
- 6) If the procedure involves the potential to produce an aerosol (e.g. involves vigorous shaking, mixing, homogenisation or ultrasonic disruption), it must be performed in a safety cabinet. These are located in;
GHRC - . labs 2, 4, 6, 8, 11, and 13 (Medical Research Unit); and rooms 1/017 (SIFT lab), 1/019 (Incubator Room), 2/001 (Molecular Lab), 2/002 (Histology), 2/006 (Biomaterials), 2/010 (Magnetics), and the Cell Therapy Suites.
Huxley – Rm.152b, Rm.152c, Rm.155b, Rm.206, Rm.311
Mackay – DT3
- 7) All other aspects of the procedure should be performed in a fume hood or other suitable sterile area.

Techniques

- 1) Before handling any tissue ensure that appropriate training has been received in handling reagents associated with specimen handling. If unsure contact a responsible person.
- 2) Where possible, process samples in batches. This reduces the time spent handling human material.
- 3) Where possible minimize the use of sharps in any procedure involving human material e.g.
 - a. Glass pipettes, scissors, scalpel blades, dissecting forceps.
- 4) . To minimize risk in the event of spillage or breakage do not store sharps in designated handling areas.
- 5) Wash your hands frequently during the course of your daily work and always before a break and at the end of the day.
- 6) Wash hands immediately if they become, or suspect they have become, contaminated by a sample.
- 7) As infection can occur by parenteral (diffusion through the intact skin, diffusion through mucosal membranes, inhalation) inoculation, it is of paramount importance that when handling infectious material, contamination of surfaces is controlled. For instance
 - a. Existing cuts and abrasions and other skin lesions are properly protected and accidental self-inoculation and splashing of mucous membranes be avoided.
 - b. Any puncture wound must be treated immediately by encouraging bleeding and liberally washing with soap and water.
 - c. Puncture wounds or contamination of mucous membranes or broken skin must be reported promptly to the Head of Department, Senior Laboratory Staff and Consultant Microbiologist (Dr George Orendi, Central Pathology Laboratory) and recorded by the person responsible for the work.

Training requirements for users of human tissue samples

1. Only staff that has completed adequate training are permitted to handle human material.
2. Staff must have attended a formal induction into the procedures of the Guy Hilton Research Centre or Huxley building prior to undertaking any work.
3. Staff must also complete the Human Tissue Induction. This will generally occur as part of the normal induction process. If investigators move into Human Tissue work later on this induction can be found on the Research Governance Website as the HTA-40 document. A copy of the form should be sent and acknowledged by the local Human Tissue Officer before work can be commenced.
4. Staff should have completed an entry for the human tissue users register (HTA-42) in conjunction with their principal investigator and ensure they have been cleared to work by occupational health prior to beginning work. Copies of this form and its associated SOP can be obtained via the Keele University Research Governance website.
5. Staff must agree a training schedule for their handling of their human prior to commencing work. This training schedule should be formally documented using the HTA-43 Human Tissue Logbook. This must be sent to the local Human Tissue Officer for review. Copies of this form and its associated SOP can be obtained via the Keele University Research Governance website.
6. Staff working with human tissue must either have attended, or registered to attend one of the central *Human Tissue Act Training* sessions held at the Learning Professional and Development Centre Sessions last two hours and cover the history of the Human Tissue Act as well as the local procedures for acquiring, storing, using and disposal of human materials. Those performing procedures involving human material must either have attended, or registered to attend the next available session, prior to starting work. Staff can register on these courses using the learning and professional development section of the *Keele People* Website.
7. Staff who are working in a project in which consent is obtained by the research team must attend the *NIHR Good Clinical Practice Training*. A copy of the certificate of completion must be sent to the local Human Tissue Officer to evidence this training.
8. Those staff who are inexperienced in acquire consent from research participants must not perform this independently until they have undertaken both the Good Clinical practice training and have been supervised by a Principal Investigator who has experience in obtaining informed consent, or alongside a trained clinician. This supervision must be fully logged onto the HTA-43 training logbook and acknowledged by a local Human Tissue Officer before staff are allowed to acquire consent on their own.

Protective Equipment

Personal protective equipment (PPEs) must be used throughout procedures involving human tissue.

Always contact a senior staff member if unsure of level of protection required.

Individual standard operating procedures (and attached risk assessment documents) determine specific levels of protection required. These include:

Generic

- 1) Short trousers are not permitted.
- 2) Open-toed footwear is not permitted.
- 3) Long hair (shoulder length or greater) should be tied back.
- 4) Decorative accessories should not be worn in a designated Human Tissue Handling laboratory. These items should be stored in a safe, locked place until the completion of the procedure. These may include;
 - a) Earrings
 - b) Bracelets
 - c) Necklaces
 - d) Rings.
- 5) Always cover exposed skin abrasions with a waterproof dressing.
- 6) Never mouth pipette in any laboratory area.
- 7) Never lick labels in any laboratory area.

Personal

1 Gloves:

- a. Always use disposable gloves when handling human material.
- b. Wearing two pairs of gloves will reduce the risk of skin contact but should be performed on an ad hoc basis where instrument handling sensitivity is not compromised.
- c. Replace gloves as soon as they become visibly soiled, torn or punctured.
- d. Gloves that have been used in the handling of human material must be discarded before handling anything outside the designated area.
- e. Used gloves must be disposed of safely into yellow bags.
- f. Latex and hypoallergenic gloves are available in all designated Human Tissue Handling and non-designated laboratories.

2 Laboratory Coats:

- a. Long-sleeved Howie-type coats must always be worn when handling human samples.
- b. These are stored in, or adjacent to, designated Human Tissue Handling laboratories.
- c. Non-protective garment sleeves should not protrude beyond the cuffs of the coat.

3 Aprons:

- a. Plastic aprons must also be worn when homogenising human material.
- b. These are stored in designated laboratories.
- c. Aprons must be discarded before handling anything outside the safety cabinet.
- d. Aprons must be discarded before leaving designated laboratories.

4 Facial barrier protection

- a. These must be used whenever;
 - i. splashes
 - ii. sprays
 - iii. droplets
 - iv. aerosols
 - v. may be generated.
- b. Available types include
 - i. chin-length face shields
 - ii. masks
 - iii. hood sashes
- c. Face Barrier protection is stored in designated laboratories.
- d. Note that opening some containers may create aerosols.

Environmental contamination control

- 1) During the work full attention must be given to the control of splashing and contamination of the bench area and care must be taken to avoid the transfer of human material to equipment and surfaces.
- 2) These must, as a matter of course, be disinfected as soon as possible after use and immediately if contamination is suspected.
- 3) Using fresh gloves, the specimen handling area must be washed down thoroughly with freshly prepared disinfectant using disposable paper towels.
- 4) Dispose of these safely (see relevant sections under 'Disposal/Decontamination and 'Disinfectants').
- 5) If a leaking or broken specimen arrives, do not touch it or any others on which it has leaked.
 - a) Ask a senior member of staff to deal with it.
- 6) Leaking specimens must be sent for immediate safe disposal. Exceptions to this are;
 - a) When it is not possible to obtain a repeat it may be necessary to rescue the material.
 - b) When it is impracticable to obtain a repeat it may be necessary to rescue the material.
 - c) Specimen rescue must be attempted only on the authority of senior staff.

Safety cabinets

Chemical fume hoods are designed for working with chemicals that produce fumes. Air enters through the front opening of the hood and exits through an exhaust duct without being filtered. A chemical fume hoods protect the worker but not the product or the environment.

A microbiological safety cabinet is defined as a cabinet intended to offer some protection to the user and the environment from the hazards of handling infected material and other dangerous biological material but excluding radioactive, toxic and corrosive substances, any air discharged to the atmosphere being filtered (British Standard 5726: 1979 - revision in preparation). E.g. HEPAIRE BS5726 1979 CLASS I cabinets.

A Class I cabinet is an open-fronted exhaust protective cabinet, which can be used for all except Hazard Group 4 pathogens. Potentially infectious airborne particles will be contained within the cabinet and retained by impaction on a filter. Put simply the Class 1 cabinet protects the worker but not the product. The cabinet must exhaust through a HEPA filter to the outside air. Regular maintenance and performance checks will help to ensure against mechanical faults and substandard performance.

A Class II cabinet is the most common safety cabinet found in clinical laboratories. In a Class II cabinet air enters the cabinet, mixes with filtered cabinet air, and passes through intake grilles at the front of the cabinet. The air mixture is drawn up in an enclosed area (the plenum) behind the work space to the top of the cabinet. Seventy percent of the air mixture is pushed through the high-efficiency particulate air (HEPA) supply filters into the cabinet work area; the remaining 30% of the mixture is pushed through the exhaust HEPA filters. Class II cabinets protect the worker, the product, and the environment from contamination. Class II cabinets are not suitable for working with chemicals.

A Class III cabinet is used when dealing with highly infectious agents.

1. All procedures involving handling human material where aerosols may be generated (e.g. during vigorous shaking, mixing, homogenisation or ultrasonic disruption) must be performed in Cat II biological safety cabinets (located in labs K10 and K12, Keele Building).
2. The area must be cleared of any unnecessary equipment before work starts.
 - a. Apparatus and material in use in the cabinet during its operation must be kept to a minimum and placed so as not to disrupt airflows (check with anemometer if additional equipment is placed in the cabinet).
3. Access of unauthorised persons to the proximity of the work must be controlled to ensure that the person carrying out the work is free from interruption or accidental contact with others, and that disturbance of the airflow from the safety cabinet is minimised.
4. The cabinet must never be used unless the fan is switched on and the airflow indicator is in the safe position after a five minute "warm up" period.

- 5 Check the airflow monthly with vane anemometer. Record the values of five positions in record book/on record sheet and initial (see record book/chart for positions).
- 6 The openable glass viewing panel must not be raised when work is in progress in the cabinet.
- 7 Centrifuges must never be placed in Class I cabinets.
- 8 All work must be performed well inside the cabinet and be in sight through the glass screen. In Class I cabinets larger items must be placed towards the rear.
- 9 A bunsen burner or other naked flame must not be used in the cabinet. The heat generated may distort the airflow and the filters may be damaged.
- 10 The cabinet fan must be run at least five minutes after completion of work in the cabinet.
- 11 After a working session;
 - a. The working surfaces must be wiped with a disinfectant.
 - b. The wire grids protecting the prefilters must be examined and wiped clean with a disinfectant-soaked cloth. Grids and filters can become heavily loaded with dust without significantly affecting the airflow, but if such particles are dislodged they may prevent a hazard.

During maintenance of safety cabinets (which includes outside contractors) a notice must be attached to the front of the cabinet prohibiting its use. All staff must also be informed of scheduled maintenance at least two weeks in advance.

Leakages

- 1) In the event that a container used to transport a Human Tissue Sample is found to be leaking the leak should first be minimized by placing the sample onto/into either a large plastic tray or large plastic beaker. Glass beakers should not be used to minimize breakage risk.
- 2) Prevent access to others and maintain control of the contaminated area.
- 3) Seek the advice of the Safety Officer or deputy before trying to recover leaking or broken specimens.
- 4) In the event that it is suspected leakage may have occurred on route;
 - a. Couriers, if used, must be notified immediately.
 - b. Representatives at the site of origin must be notified.
 - c. If sample has been delivered by hand from a local laboratory the route of delivery must be retraced and potential leakage sites cleared and decontaminated.
- 5) Then;
 - a. Follow procedures outlined for Spillages were major leaks have occurred which are readily visible.
 - b. Once major leaks have been absorbed and removed then decontaminate the entire area where potential leaks may have occurred.
- 6) Leaking specimens must be sent for immediate safe disposal. Exceptions to this are;
 - a. When it is not possible to obtain a repeat it may be necessary to rescue the material.
 - b. When it is impracticable to obtain a repeat it may be necessary to rescue the material.
 - c. Specimen rescue must be attempted only on the authority of senior staff.

Leaking Sample Recovery Protocol

- 1) Place container or specimen on a containment tray and take to a safety cabinet.
- 2) Remove lid or cap and transfer the remaining part of the specimen to another container.
- 3) Replace cap and place soiled container in a plastic bag and leave it on the tray.
- 4) If the request form is soiled, place it in another plastic bag and put the bag on the tray so that somebody else can copy the information.
 - a. When dealing with contaminated request forms/lab books/other paperwork
 - i. Wear disposable gloves
 - ii. Dictate information on form/paper/etc to colleague who will complete a new form
 - iii. Discard the contaminated paper into an infected waste container
- 5) Transfer the plastic bags containing the broken/leaking container and form into an appropriate container for disposal and disinfect the tray.
- 6) Finally, disinfect or sterilise the tray or container in which the affected specimen(s) arrived in the laboratory.
- 7) Begin processing Human Tissue Sample according to relevant Standard Operating Procedure.

Breakages

- 1) In the event of a specimen container breakage first action is do not touch it or clear up the mess.
- 2) Second action is to prevent access to potentially contaminated area.
- 3) Then;
 - a) Stay with the specimen to prevent other people touching it.
 - b) Ask for help from senior staff.
 - c) If senior staff is unavailable prevent access to contaminated area and seek help.
 - d) Report the incident to your supervisor as soon as possible.
- 4) Once the above steps have been performed the Standard Operating Procedure to decontaminate and recover a breakage site is to;
 - a) Cover with an absorbent paper towel and soak in 10% hypochlorite solution.
 - i) 10% hypochlorite solution is available in all designated handling areas.
 - b) Leave for 30 minutes.
 - c) Remove towel and any broken items into a metal container using forceps and wearing rubber gloves.
 - i) Autoclavable containers are available in all designated handling areas.
 - d) The container and its contents must then be autoclaved.

Major Spillages

In the event of a major spillage:-

1) **GET HELP**

- a. Inform your Supervisor who will in turn inform the Safety Officer or his Deputy. The Safety Officer will decide whether to operate the information cascade system.

2) **DO NOT ATTEMPT TO DEAL WITH THE SITUATION ALONE.**

3) **The Safety Officer or his Deputy will;**

- a) Seal the area.
- b) Identify the hazard/hazards.
- c) Carry out an immediate risk assessment having due regard for:
 - i) Whether the building needs to be evacuated.
 - ii) Whether expert help and advice is required.
- d) Advise staff who may have become contaminated.
- e) Advise and co-ordinate the decontamination procedure having due regard for:
 - i) The level of personal protective equipment needed.
 - ii) The appropriate disinfection method required.
- f) The Safety Officer having consulted with the Head of Department and others as appropriate will decide when the area can be reopened.

Small Spillages

- 1 In the event of a specimen spillage first action is do not touch it or clear up the mess.
- 2 Second action is to prevent access to potentially contaminated area.
- 3 Third action is to remove potentially contaminated protective garments and replace with new ones.
- 4 Then;
 - a. Stay with the specimen to prevent other people touching it.
 - b. Ask for help from senior staff.
 - c. If senior staff is unavailable prevent access to contaminated area and seek help.
 - d. Report the incident to your supervisor as soon as possible.
- 5 Once the above steps have been performed the Standard Operating Procedure to decontaminate and recover a spillage site is to;
 - a. Ensure that persons involved in clearing spillage all wear gloves and goggles.
 - b. Cover spillage with spillage granules.
 - i. Spillage granules will absorb up to 100% of their weight.
 - ii. Spillage granules are stored in, or immediately adjacent to designated handling areas.
 - c. Once granules have absorbed spillage use the provided disposable brush and pan to collect and clear granules into an autoclave bag.
 - d. Check with a senior member of staff over suitability of spillage liquid for autoclaving.

Labelling human tissue samples

1. All human tissue samples must be labelled clearly and legibly with the following information:

i) **A unique Sample ID** – every sample aliquot must have a unique identifier which can be used to track it through the stages of its acquisition, use and disposal from the licensed sites. The Unique ID should begin with the Principal Investigators Initials to facilitate sample identification, and then a unique alphanumeric string should be used to uniquely identify each individual aliquot.

ii) **Species and cell/Tissue Type** – tissues must be identified as being of human origin, and must also contain detail of the cell/tissue stored. Details of cell number or concentration should also be recorded.

iii) **Date sample received/derived** - The date which the samples were acquired or derived from the original tissue sample should be recorded.

This information must match with what is recorded in the HTA-8/9 logbooks for these tissue samples

2. Sample aliquots should be held in boxes, racks or other secure containers. These containers should be made of a material durable enough to provide physical protection to the samples at the temperature at which they are stored. Samples should be arranged in an organised manner within these containers (e.g. in ascending Sample ID number or date of collection) to facilitate ease of auditing as well as providing an additional back-up for identification if a label is damaged.

3. The outside of the container should be legibly and securely labelled with the following information:

i) *Study name/identifier*

ii) *Species and cell/Tissue Type*

iii) *Start and end dates for the research study*

iv) *Name of Principal investigator (and user)*

iv) *Details of Biological and Chemical Hazards that may be contained within*

If multiple boxes for a study, then there should be an indication of the samples contained within each box by unique sample ID number.

4. Researchers should regularly check the labelling of the samples and containers to ensure that labels have not been smudged or degraded. If they have been this must be corrected immediately. If a sample has become unidentifiable this must be reported as an adverse event using the HTA-32 adverse event reporting system.

5. Users should ensure that they clearly understand the labelling and hazard warning labels used on specimens before handling them. If unclear contact source for clarification before proceeding with handling.

Logging the storage of human tissue samples

1. When relevant materials arrives it must be logged electronically using the HTA-8 (for human tissues) and/or HTA-9 (for primary human cells) spreadsheets. The spreadsheets and their associated SOPs can be found on the research Governance website.
2. Details found on the label of the tissue sample should directly correspond to the information present in the HTA-8/9 logbooks
3. Any cells derived from the originally-received human tissue sample must be logged as a derived material on the HTA-8 spreadsheet, and the cell samples themselves logged as a separate entry on an HTA-9 spreadsheet.
4. A copy of these spreadsheet should be held securely by the Principal Investigator and another dated copy sent immediately to the local HTA officer (either Alan Harper (GHRC) or Dr Dan Tonge (Huxley).
5. Users should send updates to the HTA officer when additional materials are acquired, or when previous materials are disposed or removed from the building. Principal Investigators will be emailed every 2 months requesting an update of their spreadsheets, or to provide a statement that there is no change in holdings since the previous update.
6. Samples consisting of human material must be stored in designated rooms and storage locations (contact local HTA officer for details). The exact environment and storage location must be described in the HTA-8 or HTA-9 spreadsheets.
7. Samples intended for human application should be stored separately.

Packaging and transporting Human Tissue Samples

As part of the requirements of the Institute for Science and Technology in Medicine (ISTM) holding a Human Tissue license (#12349), we are required to utilise a quality management system to ensure that all research projects use appropriate procedures for the acquisition of human tissues. Acquisition of tissue often does not occur within our research sites and as such this necessitates the transport of human tissues either locally, nationally or internationally. The transport of human tissue introduces risks of damage to the tissue itself as well as risk of exposure to biological and chemical hazards to those transporting it as well as the general public if packaging should fail. Projects involving transportation of human tissue should also detail their specific process for transportation as part of their project standard operating procedures, as well as document a risk assessment of their transport processes as part of their project risk assessment (HTA-31).

The *The HTA-36 Transportation of human tissue sample* standard operating procedure sets out the processes that must be followed when transporting human tissue between research sites to help minimise the risk of any of damage to tissues or individuals who may come into contact with it during transportation. Transportation can occur over a range of differences. will set out the regulations covering transportation from shortest to longest distances.

Transfer of human tissues between laboratories within the Huxley or Guy Hilton Research Centre (GHRC)

- 1.** Prior to transportation between labs, researchers should know the location of materials for cleaning and decontaminating spillages, as well as the nearest appropriate clinical waste disposal route to ensure that spillages can be dealt with promptly, efficiently and safely.
- 2.** Transportation of human material between laboratories must be performed using suitable breakproof and spillproof containers. Containers should be made of materials that can be easily disinfected in the case of spillage. These should have secure lids which can be tightly sealed. Tissues should not be carried directly in gloved hands, pockets or loose inside bags.
- 3.** Samples held in Eppendorfs, test tubes or other round bottomed containers should be placed in a rack to hold the samples in an upright position to help prevent them from being damaged upon transfer.
- 4.** Researchers transferring samples between laboratories should be wearing full personal protective equipment as appropriate for the handling of these tissues. Researchers should ensure that when transferring samples fresh gloves are worn to reduce the chances of contaminating door handles, and the researcher should either have someone accompany them to open doors or they should leave one hand ungloved to do this for themselves. This ungloved hand must then be gloved immediately at the destination prior to further handling of the tissue samples.

Local transfer of tissues from UHNM to Huxley or GHRC, or between Keele licensed buildings.

1. Transfer of human tissues must only be performed after consultation of the local Human Tissue Officer (a.g.s.harper@keele.ac.uk (GHRC) or d.p.tonge@keele.ac.uk (Huxley)).
2. Prior to transfer, any researcher handling the samples should have read the project SOP and risk assessment to ensure that they have familiarised themselves with all the necessary procedures and risk associated prior to undertaking transportation. They should also have read all relevant regulations (including this SOP) to ensure that the correct procedures are followed.
3. Within the environment of the UHNM, Tissue samples must be transported by the UHNM courier service when transportation either requires vehicular transport on UHNM roads or use of public roads.
4. Local transfer by staff using vehicles other than UHNM courier must only be performed if it is either inappropriate or impractical to use UHNS courier through the need for immediate transfer, transfer during unsociable hours or the lack of UHNM courier availability at the required time
5. Local transfer by staff using vehicles other than UHNM courier can only be performed when a risk assessment approved by senior staff (specified in 2.2.1) has demonstrated that there is limited risk of harm to tissue sample, to the staff member transporting the sample or the general public who could be exposed to the sample in the case of a crash. If the risk is deemed too high, the research team must use an appropriate courier for the transfer of the human tissue sample. Researchers should ensure that the courier's SOP for transport will ensure the integrity of the human tissue sample and will be compliant with the Human Tissue Act as well as the HTA's codes of practice.
6. Staff members transferring tissue using vehicles other than the UHNM courier should ensure that the sample are at no time either left unattended or in the care of anybody other than a member of the research team.
7. Local vehicular transfer must only be performed using approved crash-proof packaging and a properly insured vehicle.
8. If tissue is being held in containers with screwcaps these should be taped shut to prevent leakage.
9. Each Human Tissue sample should be labelled with a unique sample identification number to facilitate traceability of the tissue from sender to receiver, a date of collection of the tissue, the initials of the principal investigator, a description of the species and cell/tissue type, and any preservative or medium it is held within and the date of packaging. Samples should not be labelled with any donor information in an uncoded format.
10. All sample labels should be waterproof and legible. If handwritten, it must be written in permanent ink.
11. Samples being transported at different temperatures must be transported in separate packages.
12. Human Tissue samples should be packaged in line with the World Health Organisation's "*Guidelines for the safe transport of infectious substances and diagnostic specimens*". This specifies a triple packaging system consisting of:

- a primary, leakproof, watertight container holding the sample. This receptacle should be wrapped in enough absorbent material to absorb all liquids in case of breakage of the sample.
- a secondary, durable, leakproof, watertight container in which to enclose and protect the primary receptacle. Multiple primary containers may be placed inside a single secondary container. Details of all the samples contained within, the shipper and the receiver should be placed in a waterproof bag and taped to the outside of this container.
- Outer shipping packaging which should be waterproof and of sufficient strength to protect the sample from physical forces. If dry ice is being used, the packaging must allow the release of carbon dioxide gas as the dry ice sublimates to prevent rupture. The outer packaging should also be labelled with a human tissue hazard warning label (UN 3373), as well as any hazard warning labels relating to the medium or preservative it is transported in (e.g. formaldehyde or dry ice).

13. To ensure that the traceability of the tissue during transfer, a list of the number, and type of samples to be transported should be sent to the receiving institute. This list must be acknowledged prior to any samples being sent. The sending institute should then log the samples actually sent, and the receive institute should cross-check this against the list. These logs should be cross-referenced by both institutes upon arrival of the tissue at the destination to ensure that all samples have been safely received. Copies of these logs of both institutes should be stored securely for auditing purposes.

14. If samples are found to have been lost on transport, this should be logged as an adverse event and the instances surrounding this should be investigated by the human tissue officers of both institutes. Corrective and protective actions should be put in place before further samples can then be sent.

Import or export of human tissue samples to/from external locations within the UK or overseas.

1 Staff planning projects involving the import and export of human tissue from outside of the UK must contact the Human tissue officer (Alan Harper; a.g.s.harper@keele.ac.uk) prior to sending or receiving tissue samples. Researchers should ensure that these activities are undertaken in accordance with HTA's code of practice on import and export of human tissues (see references). Export of human tissue may also require the additional approval of the relevant authorities (e.g. UK stem cell bank)

2. Acquisition of human tissue samples from non-commercial sources external to Keele University of UHNM must be conducted under a material transfer agreement.

3. All Material Transfer Agreements (MTA), Materials Use Licenses (MUL) or Memorandum of Understanding (MOU) must be undertaken through and with the guidance of the Directorate of Engagement & Partnerships at Keele University (<https://www.keele.ac.uk/admin/directorateofengagementpartnerships/>).

Staff should contact Clare Stevenson (Academic Legal Services Advisor, IC2, Keele University, Keele, ST5 5NH; 01782-734491; c.stevenson@keele.ac.uk) to discuss the requirements of their research project.

4. Prior to sending out or receiving human tissue samples, any researcher handling the samples should have read the project SOP and risk assessment to ensure that they have familiarised themselves with all the necessary procedures and risk associated prior

to undertaking transportation. They should also have read all relevant regulations (including this SOP) to ensure that the correct procedures are followed.

5. Investigators should also make themselves aware of the regulations covering the transportation of hazardous materials by road, rail, air and sea, and these rules must also be followed in addition to those set out here.

6. If tissue samples are being imported for use at Keele University, the research team must obtain assurance that these samples have been obtained in an ethical manner under written informed consent. Researcher's should gain documentation that consent and ethical approvals has been obtained and is held by the supplier prior to the acquisition of tissue samples. This requirement should form part of any material transfer agreement.

7. The import and export of Human Samples defined as Relevant Material (Human Tissue Act 2004) must be through authorized shipping agents (Keele commonly uses DHL). Researchers should ensure that the courier's SOP for transport will ensure the integrity of the human tissue sample and will be compliant with the Human Tissue Act as well as the HTA's codes of practice.

8. Upon delivery a sample should be immediately checked for integrity of the packaging. If the packaging is leaking or damaged then the samples should only be opened in a biological safety cabinet by trained personnel wearing appropriate personal protective equipment. The handling of these parcels is covered in the HTA-4 SOP ("Handling Broken or Leaking Specimens"). An adverse event report should be submitted for any sample in which the integrity of the packaging has been compromised.

9. If after opening the integrity of the sample has been found to be compromised, these should be disposed of utilising the procedures outlined in the disposal SOP (HTA-36). An adverse event report should be submitted for any occurrence in which the transportation of the human tissue has found to have damaged the tissue integrity.

10. The export of Human Samples must only occur if approvals to export are explicitly obtained during the Informed Consent process and have been subjected to ethical approval. The acquisition of these must be documented as part of the material transfer agreement.

11. If tissue is being held in containers with screwcaps these should be taped shut to prevent leakage.

12. Each Human Tissue sample should be labelled with a unique sample identification number to facilitate traceability of the tissue from sender to receiver, a date of collection of the tissue, the initials of the principal investigator, a description of the species and cell/tissue type, and any preservative or medium it is held within and the date of packaging. Samples should not be labelled with any donor information in an uncoded format.

13. All sample labels should be waterproof and legible. If handwritten, it must be written in permanent ink.

14. Samples being transported at different temperatures must be transported in separate packages.

15. Human Tissue samples should be packaged in line with the World Health Organisation's "*Guidelines for the safe transport of infectious substances and diagnostic specimens*". This specifies a triple packaging system consisting of:

- a primary, leakproof, watertight container holding the sample. This receptacle should be wrapped in enough absorbent material to absorb all liquids in case of breakage of the sample.
- a secondary, durable, leakproof, watertight container in which to enclose and protect the primary receptacle. Multiple primary containers may be placed inside a single secondary container. Details of all the samples contained within, the shipper and the receiver should be placed in a waterproof bag and taped to the outside of this container.
- Outer shipping packaging which should be waterproof and of sufficient strength to protect the sample from physical forces. If dry ice is being used, the packaging must allow the release of carbon dioxide gas as the dry ice sublimates to prevent rupture. The outer packaging should also be labelled with a human tissue hazard warning label (UN 3373), as well as any hazard warning labels relating to the medium or preservative it is transported in (e.g. formaldehyde or dry ice).

16. To ensure that the traceability of the tissue during transfer, a list of the number, and type of samples to be transported should be sent to the receiving institute. This list must be acknowledged prior to any samples being sent. The sending institute should then log the samples actually sent, and the receive institute should cross-check this against the list. These logs should be cross-referenced by both institutes upon arrival of the tissue at the destination to ensure that all samples have been safely received. Copies 7

17. If samples are found to have been lost on transport, this should be logged as an adverse event and the instances surrounding this should be investigated by the human tissue officers of both institutes. Corrective and protective actions should be put in place before further samples can then be sent.

Record keeping

- 1) All records relating to transport of Human Samples must be maintained by the Chief/Principal Investigator of the associated study.
- (2) It is the responsibility of the Chief/Principal Investigator to ensure that these records are maintained in a clear and legible manner.
- (3) All records relating to transport of Human Samples must be maintained by the Chief/Principal Investigator of the associated study in a secure and safe environment.

Disposal of Human Tissue Samples and Associated Materials and Decontamination Procedures

Detailed Procedures can be found in the *HTA-34 cleaning and decontamination* and the *HTA-38 disposal of human tissue sample* standard operating procedures. These are available for download from the Research Governance website. Investigators should also read the the Human Tissue Authority's (HTA's) code of practice on disposal (<https://www.hta.gov.uk/guidance-professionals/codes-practice/code-practice-5-disposal>). This code of practice emphasizes the need for the treatment of all human tissue as a valuable resource which must be treated with respect and with the donor's wishes in mind. Investigators should ensure the process of disposing of tissue is performed safely and sensitively.

1. Attitudes to different disposal routes vary between individuals of different cultures and religions and researchers must be sensitive to this. The proposed mechanisms of disposal and the reasons for this should be clearly communicated to the donors prior to consent for use of the tissue being obtained. When deciding on the disposal route the wishes of the donor should be a central consideration, and alternative methods for disposal should be accommodated as far is safe and practical. Donor wishes should be recorded on the consent form.
2. If tissue is from a deceased donor, the wishes of the relatives should be considered when disposing of the human tissue samples.
3. If relevant material is imported from non-commercial sources outside of the university, then the method of disposal should be chosen as specified on the material transfer agreement.
4. Disposal of tissue should be minimised as far as is practical. However, tissue may need to be disposed of due to:
 - The ethical approval or consent for a given sample stating that it must be disposed of at the end of the research project
 - Sample is damaged, contaminated or fails quality assurance tests
 - The donor withdraws consent for the use of the sample in research
 - Being a health and safety risk to research staff
 - Material is surplus to requirement
5. The reason for disposal should be recorded in the "disposal" box on the HTA-8 or HTA-9 logging spreadsheets along with the date of disposal, method of disposal and the staff member responsible for disposing of this tissue.
6. If disposal was due to damaged caused to the tissue due to an adverse event (e.g. freezer malfunction), then the research team must complete and submit an adverse event reporting form to the human tissue officer such that corrective and preventative actions can be put in place to prevent this occurring again in the future.
7. Any information which can be used to identify the donor of the tissue sample should be removed prior to disposal.
8. For disposal of *bodily fluid samples or small tissue samples*, sample bottles and any remaining sample from the patient (including red cells, urine, etc.) must be first

decontaminated in 1% Virkon Solution overnight. Decontaminated Samples can then be disposed of in Clinical waste bins (yellow, labelled bi liners) for incineration.

9. For disposal of large organ section, the tissues should be securely packed in a yellow disposable bag, and then taken back to the hospital ward where the tissue was taken from. It will then be disposed of following the well-established procedure carried out by the ward (incineration). The details of the disposal must be documented in the HTA data base.

10. Relevant material should be bagged separately from other clinical waste, but does not need to be separately incinerated.

11. Disposable gloves, plastic aprons, blood sample bottles, disposable plastics (e.g. tubes, pipette tips, culture flasks, etc) should be decontaminated and yellow-bagged and treated as clinical waste.

Disposal of Associated Materials

- 1 Disposable gloves.
 - i Clinical waste bins (yellow, labelled bin liners) for incineration.
- 2 Plastic aprons.
 - i Clinical waste bins (yellow, labelled bin liners) for incineration.
- 3 Disposable Plastics (tubes, pipette tips, culture flasks, etc).
 - i Decontaminated then Clinical waste bins (yellow, labelled bin liners) for incineration.
- 4 Disposable Glassware.
 - i Decontaminated then Clinical waste bins (yellow, labelled bin liners) for incineration.
- 5 Sharps (needles, scalpel blades, etc).
 - i Sharps bin followed by incineration.
- 6 Blood sample bottles.
 - i Decontamination then Clinical waste bins (yellow, labelled bin liners) for incineration.
- 7 Excess human material (tissue, blood, etc).
 - i Decontamination then Clinical waste bins (yellow, labelled bin liners) for incineration.
- 8 Contaminated bench wipes, paper tissues & other disposable paper.
 - i Clinical waste bins (yellow, labelled bin liners) for incineration
- 9 Contaminated equipment
 - i Re-usable equipment (e.g. homogenisers, scalpel blade holders, scissors, pipettes).
 - Disinfection and autoclaving if possible. If not then one or other.
 - ii Safety cabinets.
 - Disinfection
 - iii Contaminated lab coats, freezer gloves.
 - Autoclaving followed by laundry (if possible).
 - iv Re-usable glassware.
 - Disinfection and autoclaving if possible. If not then one or other.
- 10 Bench tops.
 - i Disinfection.
- 11 Contaminated solutions.

- i Disinfection and autoclaving.
- 12 Solvents (e.g. phenol/chloroform/isoamyl alcohol).
 - i Waste solvent bottles.

Equipment decontamination

Centrifuge Decontamination

- 1) Routine Procedure
 - a) Whenever sample containing human material must be centrifuged in sealed centrifuge buckets, preferably with 'see-through' tops.
 - b) Always balance containers and buckets. (Centrifuge buckets and trunions must be paired by weight)
 - c) The centrifuge must be inspected after each run for signs of spillage.
 - d) The centrifuge must be inspected weekly for signs of wear defects/corrosion/cracks. Also check trunions and buckets are lubricated so they swing freely.
 - e) Centrifuge buckets may be routinely autoclaved weekly.
 - f) Centrifuge bowls are routinely cleaned weekly.
 - i) Gloves must be worn.
 - ii) Disinfection with 70% isopropanol.
 - iii) Wipe off with damp swab, then dry.
 - iv) Discard all swabs into autoclave waste.
 - g) Disposable gloves are used for ALL cleaning operations.
 - h) Never use centrifuges inside safety cabinet.
- 2) Suspected breakage inside sealed buckets of centrifuge
 - a) Always discuss with senior staff before attempting to salvage leaked specimens.
 - b) Wear gloves.
 - c) Remove bucket to safety cabinet before opening.
 - d) Disinfectant or autoclave bucket and lid.
 - e) In the event of a known spillage/breakage within the sealed bucket, this should be removed and autoclaved immediately.
- 3) Breakages outside sealed buckets
 - a) Evacuate the room and leave for at least 2 hrs (to reduce aerosol risk).
 - b) Inform senior member of staff.
 - c) A designated senior staff member, wearing appropriate protective clothing (gloves, Howie coat, face mask) will proceed with the disinfection protocol.
 - d) Turn off centrifuge at mains.
 - e) Remove any broken glass with thick gloves, forceps or swabs and dispose of safely.
 - f) If possible remove inside bowl to fume-cupboard preferably at the end of the day.
 - g) Thoroughly disinfect the bowl and lid with a phenolic disinfectant (metal parts) of hypochlorite solution (other sections) leave for 10 minutes. Wash and wipe with water. Allow to dry.
 - h) Buckets are recovered for disinfection or autoclaved (see above).
 - i) If glutaraldehyde is required, this must only be used by designated personnel under surveillance by the Occupational Health Department (Consult senior staff).

Class I Protective Cabinet Decontamination

This is essential prior to Cabinet maintenance.

The use of formalin vapour is restricted to the decontamination of exhaust protective cabinets prior to any maintenance procedures. This must only be performed by designated personnel under surveillance by the Occupational Health Department (Consult senior staff).

We are currently using a portable formalin vaporiser unit which incorporates two chemical bowls (Paraformaldehyde bowl and Ammonium Carbonate bowl) and two water bowls. The Paraformaldehyde is first vaporised into Formalin and the cabinet disinfected. The Ammonium Carbonate is then vaporised and acts to neutralise the Formalin vapour.

1. Put the gas generator unit inside the cabinet and the control box outside.
2. Put the paraformaldehyde 11.5g into bowl C1 (top left) and the ammonium carbonate 14.6g into C2 (top right).
3. Put 100mls of water into each of the other bowls.
4. Close up the cabinet and seal off with tape.
5. Power on and leave to run. Leave room.
6. Return after 3-4hrs.
7. Remove tape, power cabinet on, open cabinet, leave to run for 1 hr.
8. Remove vaporizer unit and wipe down with sterile water.
9. Wipe down all cabinet surfaces with sterile water first and then 70% alcohol.
10. Power down cabinet. Remove all detachable working surfaces and clean as described in (9).
11. Replace all parts, clean again.

N.B. labcoats, gloves and facemasks must be worn throughout this procedure.

Class II Protective Cabinet Decontamination

This is essential prior to Cabinet maintenance.

The use of formalin vapour is restricted to the decontamination of exhaust protective cabinets prior to any maintenance procedures. This must only be performed by designated personnel under surveillance by the Occupational Health Department (Consult senior staff).

We are currently using a portable formalin vaporiser unit which incorporates two chemical bowls (Paraformaldehyde bowl and Ammonium Carbonate bowl) and two water bowls. The Paraformaldehyde is first vaporised into Formalin and the cabinet disinfected. The Ammonium Carbonate is then vaporised and acts to neutralise the Formalin vapour.

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10. Power down cabinet. Remove all detachable working surfaces and clean as described in (9).
11. Replace all parts, clean again.

N.B. labcoats, gloves and facemasks must be worn throughout this procedure.

Record Management

The Research quality management system used by Keele University to ensure compliance with the Human Tissue Act necessitates the generation of a number of documents relating to the acquisition, storage, use and disposal of human tissue. During a research project involving the use of human tissue, the following types of documents may be created and are subject to the procedures outlined below:

- Risk Assessments relating to individual project and premises
- Standard Operating Procedures
- Donor consent form and questionnaires
- Ethical and research governance approvals
- Human Tissue Storage logs
- Material Transfer Agreements
- Human Tissue transportation and delivery records
- Records of research data, laboratory records and associated metadata
- Records of equipment maintenance, calibration and servicing
- Reports of audits of storage conditions, sample records, consent and disposal
- Records of adverse events and complaints
- Records of Staff training and health and safety assessments

To ensure we meet the standards required for HTA-licensed buildings, there must be a clear policy in place to ensure appropriate management of each of these documents. The ***HTA-39 Standard operating procedure on Record Management*** (available on the Research Governance Website) details the procedures that must be followed with regards to the creation, amendment, retention and disposal of these records.

In addition to the guidelines detailed below, all research teams must also ensure that their projects are compliant with all Keele University record management policies prior to commencement of any research project using human tissues. This includes policies relating to *data protection, freedom of information, confidential records, record retention* and *Whistleblowing* (see ***References*** below for links).

Record Creation

- 1.** Records should be created using the relevant template document and associated standard operating procedure document for each type of record. HTA related templates can be found on the research governance website
- 2.** If no template is available, additional records should be created in a standardised manner for each research project. As a minimum, these should include the project title, the name of the chief investigator, the type of document and the version number and date.
- 3.** Information that could allow the identification of the donor should only be included in an uncoded format on donor consent forms or questionnaires. Appending any donor details should be avoided on all other documentation. The types of information that should not be appended are specified in the Keele University Policy on ***Confidential Records***. If necessary, research records should only include information regarding the donor by use of a sample identification number.

1. Electronic files should be named in a manner that allows their easy identification by the entire research team as well as external auditors. For example “Document Title_Project code/name_PI surname_version date_version number” would provide a systematic approach to record naming.
2. Paper records should be completed using pen only, in a legible manner. Pencil must not be used as this could allow untraceable amendment to the document.
3. To ensure information is easy to find, avoid duplication of records as far as possible.

Record Amendment

1. If amendment of an electronic document is required then a separate file should be created with an updated version number and date associated with it to identify the progression of the file. This should be stored alongside the original document and a summary document outlining the changes made to each new version to ensure amendments to the document can be traced.
2. If amendment of a paper document is required then this should be made by putting a single line through the text to be changed and initialled to ensure auditing of the changes made. Tipp-ex or other correction fluids should not be used, nor should text be scribbled out to become illegible.

Record storage during the project

1. A project file containing all project records must be securely stored in the HTA-licensed premises in which the research is conducted. The only exceptions to this would relate to records of donor-related information held by external research partners supplying tissue under the auspices of a material transfer agreement. Written assurances of the storage of these research documents should be obtained and securely stored by the chief investigator.
2. Confidential information relating to the personal information of donors or staff must be stored according to the regulations in Keele University’s ***Data Protection*** and ***Confidential Records*** policy documents (see references for links).
3. Paper records should be stored securely in a locked filing cabinet only accessible to members of the research team. If paper records are removed from secure storage, they should not be left unattended in the absence of a member of the research team.
4. Electronic records must be stored on password-protected computers connected to the Keele computer network. Electronic files related to human tissue projects should be stored securely on Keele network drives rather than the hard disk to ensure the document can be recovered in the event of a computer malfunction.
5. Paper and electronic records should be filed in a systematic manner which should facilitate their identification both by the research team as well as external auditors.

Access to Records

1. Due to the need to protect donor confidentiality, access of research records should be controlled by the chief investigator, and should be limited to those members of their research team directly involved in conducting the research project.
2. The chief investigator of a project is responsible for supervising and monitoring the correct handling of records by the research team during the day-to-day running of the

project. However, records may also need to be scrutinised as part of audits of human tissue research projects carried out internally by the Designated Individual and Human Tissue Officer, as well as externally by the Human Tissue Authority. The chief investigator should allow access to research records at the requests of these individuals. Those concerned about disclosure of patient identifiable information should refer to the HTA guidance on disclosure of patient identifiable information (see references below)

3. As detailed under Keele University's **Data Protection** policy, donors and staff are entitled to access any personal information held about them. If a research team is approached about providing access to a donor or staff members personal data, they should refer the enquiry to the University research governance officer (n.leighton@keele.ac.uk) for assistance.

Record retention following project

1. Records relating to a specific human tissue **sample** should be retained for until its use or disposal. If data arising from the use of this tissue is to be published then records should be held beyond the use of the tissue to ensure that this can be made available for audit of this research data. The chief investigator should use the University **Records retention policy** and **Records retention schedule** (see references below for links) for exact details on how long each record must be held available for audit.

2. Records relating to a human tissue research **project** should be retained for audit beyond the end of the completion of the project. The duration of retention depends on the type of tissue and also the funder of the research. The chief investigator should use the University **Records retention policy** and **Records retention schedule** (see references below for links) for exact details on how long each record must be held available for audit.

Record Disposal

After the requisite retention period for records, they should be disposed of securely. For paper records this must occur by shredding and/or use of confidential waste disposal routes. For electronic records, the data files should be securely removed by the IT services helpdesk, as files disposed of via the recycling bin can be relatively easily restored. Further advice is available on the IT website. If computers that have held confidential records need to be disposed of these will be disposed of in line with the university policy on **electronic records**. Investigators should contact the residential Operations, CFM, who will pass the computer to Keele's accredited PC disposal agent after IT services has cleansed the computer.

Accident Reporting

Accident reporting falls under the jurisdiction of The Reporting of Injuries, Diseases and Dangerous Occurrences Regulations

Reportable accidents under the above regulations include all fatal and major injuries and any that result in inability to carry out normal work for more than 3 days. Regulation 3(2)(i) is particularly pertinent to staff in clinical laboratories.

In addition, certain dangerous occurrences defined within the Regulations are reportable. Certain incidents, diseases and dangerous occurrences have by statute to be recorded and reported directly to the Safety Executive.

As well as conforming to the specific requirements of the Regulations, a record must be kept of all injuries, diseases and dangerous occurrences which occur in the laboratory or are associated with the work in the laboratory. The record keeper (Safety Officer) must be fully authorised to follow up all such incidents or occurrences as necessary and report them to the **head of department** or authorised deputy so that suitable action to prevent recurrence can be taken. Appropriate advice can be found in the Health Services Advisory Committee (HSAC) publication "Guidance on the recording of accidents and incidents in the health services".

N.H.S. staff are also required to report incidents/accidents with equipment, reagents and other materials used at work to the Department of Health Defect Centre of the Medical Devices Directorate.

Accident report forms are obtainable from the Safety Officer. Senior staff must keep one blank copy in the Accident Report book for their section, and replace it if used.

Note: Action taken as a result of any incident is an opportunity to review working practices and minimise all risks.

Adverse Event reporting

An adverse event is defined as any event that:

- i) Causes harm or has the potential to cause harm to staff, visitors or research volunteers
- ii) Leads to or could lead to a breach of security of the premises and any relevant materials held within.
- iii) Causes harm to or has the potential to cause harm to stored human tissue samples
- iv) Triggers an internal enquiry
- v) Is in breach of the Human Tissue Act or HTA codes of practice

[Source:https://www.hta.gov.uk/sites/.../Guide_to_Completion_of_the_Tissues_and_Cell_s.pdf]

In the event of an adverse event, Staff should immediately report the incident to Technical Support staff at the Guy Hilton Research Centre (Katy Cressy or John Misra) or Huxley Building (Jayne Bromley) and then assist in corrective action that can be safely performed to minimize risk to others or damage to human tissue samples.

As soon as all reasonable actions have been performed the reporting staff member will be asked to complete Part 1 of the Adverse Event Reporting Form (HTA-32). This can be found online on the Research Governance website alongside the standard operating procedures for its use. Copies of these are also held by the technical staff in the Guy Hilton Research Centre and Huxley. This must be returned as soon as is practically possible to the Human Tissue Officer (a.g.s.harper@keele.ac.uk).

Upon receipt of the adverse event report, the Human Tissue Officer will immediately begin an investigation into the adverse event. This investigation will be recorded in Part 2 of the adverse event reporting form.

The Human Tissue Officer will request an urgent meeting with the Principal Investigator whose tissue had been the subject of the adverse event. The events surrounding the adverse event will be discussed as part of a root cause analysis, and an action plan will be agreed to try to put in place corrective and preventative analysis. This will include a review date to ensure appropriate precautions have been implemented. These plans will be signed off by both the Principal Investigator and the Human Tissue Officer, and the report sent to the Designated Individual to agree the action plan.

At the review date, the Human Tissue Officer and Principal Investigator will review the action plan to ensure all objectives have been met. If further actions are still required these will be noted and the case reviewed at a subsequent meeting. If all actions have been successfully implemented the Human Tissue Officer and Principal Investigator will acknowledge this and the report returned to the Designated Individual to acknowledge the completion of this process.

Complaints Policy

When handling a complaint, members of staff should be aware of the following guiding principles. (Adapted from *RM02: Policy and Procedures for Handling Complaints*)

- Complaints should be viewed as an opportunity to improve quality of experience for research participants and therefore should be responded to positively.
- All staff must be aware of a participant's right to comment on the standard of care they receive during their participation in a research project.
- Participants should be assured that lodging a complaint should not affect their care as part of the research project they are involved in. They should also be aware of their right to withdraw from the project at any time.
- All participants should be able to lodge a complaint regardless of their age, race, gender, nationality, religion, sexuality, level of mental or physical ability.
- Staff should treat all participants politely and with respect at all times
- All complaints should be taken seriously regardless of the staff members view of the complaint
- Response to complaints must address the substance of the complaint with the aim of satisfying the participant
- Both the participant and the research team who are being complained against should feel that any investigation has been handled impartially.

The procedure for handling complaints is fully detailed in the HTA-35 standard operating procedure available on the research governance website, alongside the HTA-35 form for completion.

1. All complaints received by staff or students working as part of a human tissue research project must be treated seriously and must be recorded and responded to promptly. Complainants must be treated courteously and respect given to their concerns.
2. Verbal complaints should be annotated onto Part 1 of the *HTA-35: Complaints Form*. It may not always be possible to complete all sections of the form (e.g. a complaint received by phone call will prevent a signature being garnered from the complainant), but this should be completed as far as is practical. This should be immediately passed onto the Designated Individual (DI) to investigate, unless the DI is the subject of the complaint. In these circumstances the complaint should be passed to the License holder (Professor David Amigoni)
3. When discussing a complaint, staff should attempt to understand the event that has triggered the complaint, when this event occurred, who was involved and what the complainants desired resolution to the complaint would be. These details should be included in the form.
4. If the staff member is able to take any steps to resolve the complaint at this point and this action should be noted on the form. If this is not possible, then the staff member should politely inform the complainant that they will pass on their complaint to the DI immediately and that they will be in contact to discuss the complaint in more detail as soon as possible.

- 5.** Written complaints should be passed directly to the Designated Individual (Prof Nick Forsyth; n.r.forsyth@keele.ac.uk) to investigate and respond to. If a written complaint is received regarding the Designated Individual, this should instead be passed to the License holder (Professor David Amigoni).
- 6.** Upon receipt of a written or verbal complaint, the DI should, as far as possible, alert the Chief Investigator of the study immediately that a complaint has been received and is being investigated. The DI should also establish contact with the complainant to discuss the incident in no more than one week. A copy of the complaint record should also be passed to the Head of Research and Clinical Governance (Dr Clark Crawford; c.crawford@keele.ac.uk) to ensure that central university are alerted to the complaint and can offer support as needed. If the DI is not available to contact the complainant within this timeframe, then the complaint should be passed to the Head of Research and Clinical Governance to instigate an investigation.
- 7.** The DI should discuss the nature of the complaint confidentially with the complainant as soon as reasonably possible either by face-to-face meeting or via phone, depending on the preferences of the complainant. The notes of this discussion should be recorded on Part 2 of the HTA-35: Complaints form. The DI should attempt to understand the incident which has led to the complaint, as well as to understand the complainant's concerns and desired outcomes.
- 8.** If the complainant is a third-party acting on behalf of the research study participant, then the DI should also, where possible, discuss the complainant directly with the participant to ensure that the complaint is made with their knowledge and consent.
- 9.** If an appropriate resolution can be found at this time (e.g. an apology) then this should be offered, and this should be indicated on the report form. The CI should be informed of the outcome of the complaint. As far as is practical the complainant, CI and DI should sign off the report form to indicate resolution of the complaint.
- 10.** If a resolution cannot be immediately offered, an investigation should be conducted. The investigation should be held discreetly with all conversations treated as confidential. The members of the research team involved in the incident as well as the CI should be interviewed. Notes of the interview should be recorded and signed off by both the DI and the interviewee. Records of these meetings as well as the report forms should be held in a secure location only accessible to the DI. If the complaint is about the DI this function will be performed by the Head of Clinical and Research Governance.
- 11.** Once the investigation has been completed, the DI or the will decide upon the action to be taken and contact both the complainant and the CI of the study to discuss the outcome of their investigation. If the complaint has been successfully resolved, then the actions will be put into practice. If the complainant remains unsatisfied, the complaint should be referred to both the License Holder to review decisions made, and amend if necessary. If the complaint is about the DI this function will be performed by the Head of Clinical and Research Governance.

Governance Policy

It is our policy to follow the procedures outlined in the Research Governance leaflet produced by Keele University's Research Services and the Code of Good Research Practice. These documents are mounted in the dedicated Human Tissue Act area of the ISTM intranet. For more information please go to <https://www.keele.ac.uk/researchsupport/researchgovernance/codeofgoodresearchpractice/>

It is our policy to also follow the procedures outlined in the University Hospital of North Staffordshire document G02: Policy on Research Governance. This document is mounted in the dedicated Human Tissue Act area of the ISTM intranet.

In the event of any issues arising please contact either Nicola Leighton (Research Governance Officer, Keele University) and/or Dr Darren Clements (UHNM R&D manager).

Staff responsible for implementing and updating procedures on Human Tissue Samples

Professor Nicholas R Forsyth

Dr Alan Harper

Dr Dan Tonge

Professor David Furness

The ISTM Human Tissue Committee reference and membership.

Membership, frequency & reporting

Title: Human Tissue Committee
Membership: Prof Nicholas Forsyth – Director of ISTM Dr Alan Harper – Human Tissue Officer Dr Dan Tonge – Human Tissue Officer (Huxley) Mr Mark Smith – Research Services Manager, ISTM Prof David Furness - Professor of Cellular Neuroscience Dr Darren Clement – UHNM NHS Trust R&D Manager
Chair: Dr Alan Harper
Sub-Groups: Health and Safety Committee
Frequency of Meeting: Annually
Receive Reports From: Health and Safety Committee Human Tissue Authority User Groups
Provide Reports To: Human Tissue Authority (in form of audit) Health and Safety Committee User Groups
Administered by: Dr Alan Harper
Terms of Reference: Attached
Authority: Keele University

Terms of Reference: - ISTM Human Tissue Committee

- 1. To implement, review, and develop the Institutes compliance with the requirements of the Human Tissue Act 2004.**
- 2. To have general oversight on research activities utilizing Human Tissues within ISTM.**
- 3. To implement and govern GLP on all research involving Human Tissues.**
- 4. To implement and govern safety procedures on all research involving Human Tissues.**
- 5. To receive and consider reports from licensing authorities and implement actions were appropriate.**
- 6. To receive and consider reports detailing safety concerns and implement actions were appropriate.**

Associated Documents

Risk Assessment form for activities involving biological agents

RISK ASSESMENT NUMBER:



CONTROL OF SUBSTANCES HAZARDOUS TO HEALTH

This form must be completed prior to the commencement of work involving a biological agent*, in order that a suitable and sufficient assessment of health risks is made. (**work involving hazardous substances requires separate assessment*)

HELP! Where a # appears, clicking on a data entry box, or on the arrow of a pull-down menu, and pressing **F1** will reveal any help available.

PART 1

Date of assessment:

Process/Activity:

PART 2
INFORMATION GATHERING FOR BIOLOGICAL AGENTS

I. Hazard Identification

NAME OF SAMPLE MATERIAL OR BIOLOGICAL AGENT(S)	HAZARD RATING# eg LOW (GROUP 1)
1	N/A
2	N/A
3	N/A
4	N/A
5	N/A
6	N/A

Note: *Include* biological fluids/tissues in the assessment- in assigning a hazard rating for these the assessor must consider the likelihood of biological agents being present. If suspected these should be listed and rated accordingly.

II. Exposure Potential

Route(s) by which exposure to the agent is hazardous to health (*see Appendix 3*):

AGENT(S) (<i>see above</i>)	EXPOSURE POTENTIAL# (<i>Appendix 3</i>)	HAZARD RATING
1	N/A	N/A
2	N/A	N/A
3	N/A	N/A
4	N/A	N/A
5	N/A	N/A
6	N/A	N/A

III. Risk

RISK=HAZARD RATING*EXPOSURE POTENTIAL

AGENT(S) (see above)	RISK
1	N/A
2	N/A
3	N/A
4	N/A
5	N/A
6	N/A

PART 3

HAZARD REDUCTION

Reducing an initial hazard could reduce the estimated risk. Answer the questions below (check boxes), if you respond "YES" to any of them complete the sections "Justify Continued Use" and "Remedial Action".

QUESTION	YES	NO	JUSTIFY CONTINUED USE	REMEDIAL ACTION
Can the use of the material be avoided?	<input type="checkbox"/>	<input type="checkbox"/>		
Can smaller amounts be used practically?	<input type="checkbox"/>	<input type="checkbox"/>		
Are there less hazardous substitutes?	<input type="checkbox"/>	<input type="checkbox"/>		

Any proposed actions may either be checked at review or will be required to be in place before approval of the assessment is given.

PART 4

CONTROL MEASURES

I. Containment Level#

Specify: N/A

Note: Work can be carried out safely on the open bench using good microbiological practice.

II. Engineering Control Measures

The work must be carried out completely in a safety cabinet* #	<input type="checkbox"/>				
*Specify location of safety cabinet and class:					
The work must be carried out in a specialised containment room*	<input type="checkbox"/>				
*Specify location of room and containment level:					
The work can be carried out partially on the open bench and partially in a microbiological safety cabinet*	<input type="checkbox"/>				
*Specify which type of enclosure is to be used and what part(s) of the work activity must be carried out within:					
Where engineering controls are used eg. microbiological safety cabinets, are these subject to a formal performance test, at least every year, and records kept?	<table border="1"> <tr> <td>Yes</td> <td>No</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	Yes	No	<input type="checkbox"/>	<input type="checkbox"/>
Yes	No				
<input type="checkbox"/>	<input type="checkbox"/>				

III. Personal Protective Equipment (PPE)

Where adequate control of exposure to the hazardous substance(s) cannot be achieved by substitution or engineering controls therefore the following type(s) of PPE will be required for part or all of the activity. **Note:** It is assumed that non-latex gloves and lab coat will always be worn.

Eye protection	<input type="checkbox"/>	Face protection	<input type="checkbox"/>	Respirator / mask	<input type="checkbox"/>
Other (eg. clothing) (specify)					
Specify when during the activity the item(s) of PPE must be worn:					

Non-disposable items of PPE must be inspected regularly and records retained for inspection

III. Emergency Procedures

	Yes	No
Written emergency instructions are available at the work site(s)	<input type="checkbox"/>	<input type="checkbox"/>
Emergency contact details are provided at the work site(s)	<input type="checkbox"/>	<input type="checkbox"/>
Disinfectants for neutralising spills of biological agent(s) are available	<input type="checkbox"/>	<input type="checkbox"/>
Proper and sufficient spill kits are available	<input type="checkbox"/>	<input type="checkbox"/>
Is the internationally recognised biohazard sign displayed?	<input type="checkbox"/>	<input type="checkbox"/>
If necessary, are specific procedures available for the safe transport of the agent(s) between laboratories or buildings?	<input type="checkbox"/>	<input type="checkbox"/>
If applicable, will a person with the appropriate expertise be available to deal with spillages of particularly hazardous biological agents*	<input type="checkbox"/>	<input type="checkbox"/>
*Specify whom and how they are to be contacted:		

The locations of the following are known to the user:

Eye irrigation point	<input type="checkbox"/>	Fire-fighting equipment	<input type="checkbox"/>	First aid box	<input type="checkbox"/>
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The user knows how to summon the following personnel:

First aider	<input type="checkbox"/>	External emergency services	<input type="checkbox"/>
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IV. Waste Disposal Routes#

Disposal/Decontamination of biological agents and contaminated equipment will be done by:

1. Clinical waste bins (<i>yellow, labelled bin liner</i>)	<input type="checkbox"/>
2. Autoclaving	<input type="checkbox"/>
3. Sharps bin followed by autoclaving	<input type="checkbox"/>
4. Disinfection Virkon <input type="checkbox"/> Bleach <input type="checkbox"/> Trigene <input type="checkbox"/> (tick as appropriate)	
5. Disinfection followed by autoclaving	<input type="checkbox"/>
6. Liquid waste storage bottle (<i>subsequent autoclaving when full</i>)	<input type="checkbox"/>

Note: Biological waste should not be disposed of in black bin liners.

V. Training

Note: Formal training will be given regarding “Local Rules” that apply to work with biological agents. A written record of attendance for all users must be kept.

Users must arrange to attend formal training

Have all users received formal training regarding work with biological agents?	Yes <input type="checkbox"/>	No <input type="checkbox"/>
Have all users received training from supervisor (or delegated staff)?	<input type="checkbox"/>	<input type="checkbox"/>

VI. Supervision

Workers **must** be aware of who their direct supervisor is for the work (in the laboratory)

Are all users aware of who will directly supervise the activity?	Yes <input type="checkbox"/>	No <input type="checkbox"/>
--	---------------------------------	--------------------------------

VII. Implications for Persons Not Involved in the Work Activity

Identify any persons in the following groups, not directly involved with the work activity, who may be at risk from the hazards of the activity.

Academic staff	<input type="checkbox"/>	Technical staff	<input type="checkbox"/>	Postgraduates	<input type="checkbox"/>
Undergraduates	<input type="checkbox"/>	Maintenance staff	<input type="checkbox"/>	Secretaries	<input type="checkbox"/>
Cleaning staff	<input type="checkbox"/>	Emergency personnel	<input type="checkbox"/>	Contractors	<input type="checkbox"/>
Visitors	<input type="checkbox"/>	Others	<input type="checkbox"/>		

Persons identified above may need to be informed, in part or in full, of the information contained in this risk assessment.

VIII. Health Monitoring

Is there potential contact with biological fluids? If yes, immunisation against Hepatitis is necessary*.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
Is an effective vaccine or other prophylaxis available/necessary for the work?	<input type="checkbox"/>	<input type="checkbox"/>
If yes, specify requirements/arrangements:		

**This should be arranged via the Occupational Health Service in the Department of Occupational Health and Safety.*

IX. Instructions for the Work Activity

All laboratory activities require precise written procedures (Standard Operating Procedure-SOP). A SOP form should be completed using information from this (*and any other*) risk assessment.

A SOP has been completed and is <u>attached</u> <input type="checkbox"/> (reference n ^o)
--

X. Repeat Risk Score Assessment

This time include control measures as determined in Part 4.

I. Exposure Potential

Route(s) by which exposure to the agent is hazardous to health (*see Appendix 3*):

AGENT(S) (<i>see above</i>)	REVISED EXPOSURE POTENTIAL# (<i>Appendix 3</i>)	HAZARD RATING
1	N/A	N/A
2	N/A	N/A
3	N/A	N/A
4	N/A	N/A
5	N/A	N/A
6	N/A	N/A

II. RISK

RISK=HAZARD RATING*EXPOSURE POTENTIAL

AGENT(S) (see above)	ORIGINAL RISK	REVISED RISK
1	N/A	
2	N/A	
3	N/A	
4	N/A	
5	N/A	
6	N/A	

XI. Accreditation and Verification of Assessment

The completed assessment must be signed and dated by the person making the assessment and then checked and signed by the senior person with responsibility for the area in which the activity is to be undertaken.

Assessor: Name _____ **Signed** _____ **Date** _____

Verifier : **Name** _____ **Signed** _____
_____ **Date** _____

An electronic copy of the assessment should be returned to the Workplace Safety Adviser.

The hard copy (with signatures) must be kept readily available where the activity is to be undertaken.

The assessment must be reviewed at regular intervals and immediately when there is any change that may affect its validity.

APPENDIX 1

Containment levels for work involving human or primate cell cultures.

HAZARD	CELL TYPE	CONTAINMENT LEVEL
LOW	Well characterised or authenticated finite or continuous cell lines of human or primate origin with a low risk of endogenous infection with a human pathogen presenting no apparent hazard to laboratory workers or to the environment. Non-human, non-primate cell lines, including those of murine origin.	Containment level 1. Good microbiological practice and good occupational safety and hygiene.
MEDIUM	Finite or continuous cell lines/strains of human or primate origin not fully authenticated or characterised, except where there is a high risk of endogenous pathogens such as blood borne viruses.	Containment level 2, plus the use of a class II safety cabinet.
HIGH	Cell lines with endogenous pathogens or cells that have been deliberately infected.	Containment appropriate to the agent.
V.HIGH	Primary cells from blood, lymphoid cells, neural tissue of human or simian origin.	Containment appropriate to the potential risk.

APPENDIX 2

Categorisation of biological agents.

From the Advisory Committee on Dangerous Pathogens (ACDP) categories for containment (*based on their ability to cause infection*).

GROUP 1 (LOW Hazard)- A biological agent that is unlikely to cause human disease.

GROUP 2 (MEDIUM Hazard)- A biological agent that can cause human disease and which might be a hazard to laboratory workers but is unlikely to spread to the community and effective prophylaxis or effective treatment are usually available.

GROUP 3 (HIGH Hazard)- A biological agent that can cause severe human disease and present a serious hazard to laboratory workers. It may present a risk of spread to the community but there is usually effective prophylaxis or treatment available.

GROUP 4 (V.HIGH Hazard)- A biological agent that causes severe human disease and is a serious hazard to laboratory workers. It is likely to spread in the community and there is usually no effective prophylaxis or treatment available.

APPENDIX 3

EXPOSURE ROUTES

Route(s) by which exposure to the agent is hazardous to health:

1=Skin, broken; **2**=Skin, unbroken; **3**=Eye Contact; **4**=Inhalation;
5=Injection; **6**=Ingestion

EXPOSURE POTENTIAL

SCORE >	1	10	100
(A) Quantity of biological agent	< 1 ml fluids 1 sample	1-10 ml fluids 2-10 samples	>10 ml fluids >10 samples
(B) Number of hazardous exposure routes (<i>from above</i>)	None	1	>1
(C) Characteristics of operation (including primary containment- <i>see notes below</i>)	Predominantly enclosed system, low chance of mishap	Partially open system, low chance of mishap	No physical barrier, any operation where chance of mishap is medium or high, aerosols produced

Notes:

- 1) Exposure Potential equals the sum of **(A)**, **(B)**, and **(C)**.
- 2) Time factors, such as frequency and duration of the activity, should also be considered. Continuous operations on a daily basis should raise the exposure estimate to the next category.
- 3) It is important that the evaluation is based only on estimates of potential exposure arising from the activity itself without additional control measures. The effect of secondary containment, such as microbiological safety cabinets, should not be included as this would pre-judge decisions on the level of containment required.
- 4) Primary containment is that containment provided by the apparatus or equipment in which the substance is handled. Secondary containment is the additional containment needed to ensure appropriate control of exposure.

APPENDIX 4
CONTAINMENT LEVELS & REQUIRED LABORATORY FACILITIES

<i>Containment Measures</i>	<i>Minimum Containment Levels</i>	
	1	2
1. Access is to be restricted to authorised persons only.	No	Yes
2. Specified disinfection procedures.	No, but disinfectants available	Yes
3. The workplace is to be maintained at an air pressure negative to atmosphere	No	No, unless mechanically ventilated
4. Efficient vector control, eg., rodents and insects.	Yes, for animal containment	Yes, for animal containment
5. Surfaces impervious to water and easy to clean. Benches to be cleaned after use.	Yes, for bench	Yes, for bench, regularly decontaminate
6. Surfaces resistant to acids, alkalis, solvents, disinfectants	Yes, for bench	Yes, for bench
7. Safe storage of biological agents	No	Yes
8. Infected material, including any animal, is to be handled in a safety cabinet or isolator or other suitable containment.	No, but procedures should minimise aerosols	Yes, where aerosol produced
9. Laboratory door to be closed during activity	Yes	Yes
10. Laboratory coats to be worn in lab. suite and removed on exiting	Yes	Yes, side or back fastening
11. Procedures for storage and maintenance of protective equipment must be in place	Yes	Yes
12. Procedures for dealing with contaminated PPE must be in place	Yes	Yes
13. Mouth pipetting forbidden	Yes	Yes
14. Eating, drinking, smoking, food storage, taking medication, cosmetic application forbidden	Yes	Yes
15. Hand wash basin in lab.	Yes	Yes, with hands-free tap operation
16. Material awaiting disinfection to be stored safely	Yes	Yes
17. Procedures for safe collection, storage and disposal of contaminated waste	Yes	Yes
18. Contaminated waste must be labelled before removal for incineration	No	Yes
19. Hands to be decontaminated immediately and on leaving lab.	Yes	Yes

20. Autoclave available for sterilisation of waste in the same building	No	Yes
21. Materials for autoclaving should be transported in robust containers without spillage	N/A	Yes
22. Incinerator for disposal of infected animal carcasses	No	Accessible
23. Adequate space for each worker (24m ³)	No	Yes
23. Accidents to be reported	Yes	Yes

Abstracted from ACDP "Categorisation of biological agents according to hazard and categories of containment" 1995, 4th edn.

COSHH assessment: Institute of Science & Technology in Medicine

Title of Experiment/Procedure:					
Date of Assessment:			Names & Status of Worker:		
Name of hazardous substances to be used	Type of Hazard Chemical or Biological Hazards identified			Approximate quantity and the likelihood of exposure, e.g. high, medium, low	
1.	NOTE: enter skin contact or absorption, eye contact, inhalation, injection, ingestion, where relevant.				
2.					
3.					
4.					
5.					
Overall risk assessment of the substances	Very high	High	Medium	Low	Carcinogen
1.					
2.					
3.					
4.					
5.					
Information source:					

Control Measures adopted (personal protective equipment)					
Biological Safety Cabinet		Fume cupboard		Good Ventilation	
<input type="checkbox"/>		<input type="checkbox"/>		<input type="checkbox"/>	
Safety Goggles	Gloves	Face Mask/ Dust mask	If special, state details		
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>		
Spillage					
Gloves	Face protection	Disinfectant	Spillage kit	Mop up	Mix with sand
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Method of Disposal					
Chemical Waste bottle	Drain	Yellow bag	Autoclave	No hazard	
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Emergency procedures					
In case of fire					
In case of water failure					
In case of electricity failure					
Emergency contact name					
Emergency phone number					
Signatures					
	Name and signature			Date	
Assessor					
Supervisor or COSHH Supervisor					

Keele University

APPLICATION FORM FOR INDEPENDENT PEER REVIEW

Instructions

The application form should be completed as concisely as possible and should address the points as applicable. Please state clearly if any section is not applicable to your project. Most of the sections are the same as the Integrated Research Application System (IRAS) form. The boxes can be expanded and text can be 'cut & pasted' to/from the IRAS form. For convenience we have indicated the relevant IRAS question numbers that map to this form.

Once your IPRC application form has been completed and signed off as appropriate, please forward an electronic copy and hard copy to IPRC Administrator, Directorate of Engagement and Partnerships, IC2 Building, Keele University, ST5 5NH, e-mail research.peerreview@keele.ac.uk.

If you have concerns regarding the disclosure of original research and the risk of plagiarism during the review process please contact the Chair of the Independent Peer Review Committee via Nicola Leighton 01782 733306.

Please note that the Independent Peer Review Committee is not linked to nor is a sub-committee of a NHS Research Ethics Committee (REC).

Note : From 1 April 2016, **Health Research Authority (HRA) approval** will be the process for applying for approvals for all research projects in the NHS led from England. Applicants should select the 'HRA approval' option in the IRAS project filter this will then automatically provide a combined application for HRA assessment and NHS REC Review (where REC review is required), which replaces the need to complete separate NHS REC and R&D application forms.

Administrative Details

Full title of the research project:

Short title of the research project:

Key words:

STATUS of STUDY (please tick all that apply)

Student Project		Feasibility/Pilot study*		Full study	
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PURPOSE OF APPLICATION TO IPRC (please tick all that apply)

For NSMI Award		For NHS REC application	
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Is this project intended/might be intended to be adopted on the NIHR Portfolio **YES/NO**

Name of Chief Investigator:

Current Post:

Contact Address:

Telephone number/Mobile number:

E-mail

Other Members of the Study Team (if there are more than 3 members please keep adding to this section)

Name:

Post:

Organisation:

Role in Study:

Name:

Post:

Organisation:

Role in Study:

Name:

Post:

Organisation:

Role in Study:

What is the principal research question /objective? Provide a clear account of the purpose of your investigation, including primary and secondary objectives (A10 of IRAS form)

Scientific background - What is the scientific justification for the research? What is the background? Why is this an area of importance? Has similar research on this topic been done before? Have all existing sources of evidence, especially systematic reviews been fully considered? What new information will it provide? (A12 of IRAS form)

Methodology (please highlight in bold as many as are appropriate) (A7 of IRAS form)

Case series/case note review	Yes / No
Case-control	Yes / No
Cohort observation	Yes / No
Controlled trial without randomisation	Yes / No
Cross-sectional study	Yes / No
Database analysis	Yes / No
Epidemiology	Yes / No
Feasibility/Pilot	Yes / No* Please see definition of pilot study at end of form
Laboratory study	Yes / No
Systematic Review/Meta-analysis	Yes / No
Qualitative Study	Yes / No
Questionnaire, interview or observation	Yes / No
Randomised controlled trial	Yes / No
Other	Yes / No
If other please give details	

Is the research being undertaken as part of an educational course or research degree? Yes / No

If yes, please provide the following details:

Name and level of course/degree:
Name of educational establishment:
Name of supervisor:

Plan of Investigation

Summary of study Give a brief synopsis/summary of methods and overview of the planned research. A flow chart or diagram should be attached where appropriate. It should be clear exactly what will happen to the research participant, how many times and in what order (A13 of IRAS form)

Timescale

Start date:

End date:

Duration:

Study population

Inclusion criteria What inclusion criteria will be used to select participants/patient records/tissue or bodily samples (list cases and controls separately if appropriate)? (A17-1 of IRAS form)

Exclusion criteria If you are excluding participants on the basis of age, sex or ethnicity please explain why (A17-2 of IRAS form)

Will the study involve the recruitment of human research participants? Yes / No

Study Setting (name and description of centres)

How will potential research participants in the study be identified, approached and recruited? (Give details for cases and controls separately if appropriate, describe sampling methodology and randomisation procedures) (A27-1, A27-2, A28, A29, A30-1, A31, A32, A33-1, A33-2, A34 of IRAS form)

Will informed consent be obtained from the research participants? Yes / No

(Give details of who will obtain consent, how it will be done, and of any particular steps other than an information sheet taken to provide information e.g. video, interactive media. If consent is not to be obtained, please explain why not) (A30-1 of IRAS form)

Subject/patient participation

(Provide details of what research participants will do e.g. treatment intervention, completion of a questionnaire, participate in an in-depth interview; provide details of how the research procedures or intervention will be administered (include duration and audit details); provide details of any risks to the participant and safeguards to be put in place) (A18, A19, A20, A21, A22, A23, A24, A25, A26 of IRAS form)

Follow-up (Provide details of follow-up procedures and time points, if appropriate)

Outcome Measures (**if appropriate**)

Primary Outcome Measure (A57 of IRAS form)

Secondary Outcome(s) Measure(s) (A58 of IRAS form)

Data Analysis

What specialist methodological advice, if any, has been sought in relation to this project?

For quantitative studies, what specialist statistical advice, if any, has been sought in relation to this project?

Has the size of the study been informed by a formal statistical power calculation? Yes / No / N/A

If YES, indicate the basis upon which this was done, giving sufficient information to allow the replication of the calculation (A60 of IRAS form)

If NO, explain how the size of the study was determined and why a formal sample size calculation is not

required

If N/A, please explain

Describe the proposed methods of analysis (identifying specific procedures in the case of statistical analysis or other analytical methods in the case of qualitative research) (A62 of IRAS form)

Where will the analysis of the data from the study take place and by whom will it be undertaken? (A41 of IRAS form)

PROPOSED EXTERNAL INDEPENDENT REVIEWERS

For full projects, **all applicants must provide names and e-mail addresses of three external independent reviewers. Reviewers must be external to North Staffordshire and wherever possible current collaborators (within the last 4 years) should be avoided. The Committee member reviewing the project may choose to send the project to one of your external reviewers, together with an external reviewer of their own choice.**

For student or pilot research projects, all applicants are requested to provide the names of three external reviewers and follow the instructions outlined above for full projects. Although these projects will normally only be reviewed by the Committee, judgment will be made by the Committee member if the project also requires external peer review.

- 1) Name:
E-mail:
Organisation:
Relationship between applicant and reviewer:

- 2) Name:
E-mail:
Organisation:
Relationship between applicant and reviewer:

- 3) Name:
E-mail:
Organisation:
Relationship between applicant and reviewer:

STUDENT PROJECTS

Names and institutional addresses of Supervisors	
Degree type and institution (if different from supervisor's)	
Potential risks and safeguards to researcher	
I can confirm that this project will be supervised in line with Research Governance requirements	Supervisor signature

	Status of Supervisor
--	-------------------------------

Principal Investigator to obtain the necessary appropriate signatures	
AGREEMENT	SIGNATURE
I confirm that the information submitted in this proposal is complete and correct and that this project will be conducted in accordance with Research Governance requirements.	Principal Investigator: Signature:
Having discussed this proposal with the applicant I confirm:- <ul style="list-style-type: none"> • that the research fits within the scientific programmes of the University / NHS Trust • that if the proposal is approved all appropriate Research Governance requirements will be met. 	<u>On behalf of the University</u> Name: Signature: Post: Faculty Research Office Director / Research Institute Director / Theme Lead / Centre Lead Programme Director / Head of Department (please delete as appropriate)
If it is a joint project between the University and the NHS Trust, or involves both the University and the Trust, signatures must be obtained from BOTH organisations.	<u>On behalf of the NHS Trust</u> Name: Signature: Post: R&D Director / R&D Manager / Academic Development Manager (please delete as appropriate)
I confirm that I have read this application and agree that if approved it will be accommodated and administered in the University / NHS Trust If it is a joint project between the University and the NHS Trust, or involves both the University and the Trust, signatures must be obtained from BOTH organisations.	<u>On behalf of the University</u> Name: Signature: Post: Faculty Research Office Director / Research Institute Director / Theme Lead / Centre Lead Programme Director / Head of Department (please delete as appropriate)

	<p><u>On behalf of the NHS Trust</u> (to be signed off by an appropriate member of NHS Management)</p> <p>Name:</p> <p>Signature:</p> <p>Post: Divisional Chair / Divisional Research Lead / Clinical Director / Lead Clinician</p>

Once this application form has been completed and signed off as appropriate please send a signed electronic copy to **IPRC Administrator, Directorate of Engagement & Partnerships, IC2 Building, Keele University, ST5 5NH, e-mail research.peerreview@keele.ac.uk**

If you have any queries when completing the application form or would like further information on the independent peer review process, please contact IPRC Administrator on 01782 734495 or e-mail research.peerreview@keele.ac.uk

***Definition of a pilot study**

A pilot study is one which acts as a precursor to a full study in order to determine the design and content of the full study. It can be used to evaluate and/or inform one or more aspects of the full study protocol. This may include:-

Methodology

Design:

- Interview schedule
- Data collection forms
- Structure of questions
- Selection of appropriate primary and secondary outcome measures

Recruitment:

- Recruitment and consent

Statistical:

- Power calculations of sample size
- Randomisation process
- Estimation of magnitude of effect of intervention

Acceptability

Likely acceptability of interventions and/or other procedures in the research process

Feasibility

- Assess deliverability
- Identification of unanticipated concerns

General issues:

Acquiring data for grant submission
Health and safety

On occasions, the pilot and full study may be presented as one application, but usually it is advisable to submit the pilot study for approval prior to consideration of the full study. If relevant, pilot studies may require power calculations and statistical analyses