Policy on Human Tissue in Research

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<td>Clinical Researchers, Divisional Directors, Clinical Service Leads, Divisional Directors of Operations, Senior Trust Managers, Service Managers</td>
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1 Policy Statement

This policy sets out how human tissue samples are to be collected, stored and used for research within the Trust.

2 Scope

The policy is relevant to any activity in the Trust involving human tissue that will be used for research purposes.

3 Framework

3.1 The use of human tissue in research is governed through a variety of rules and regulations. The main legal framework is the Human Tissue Act (2004) (the “Act”).

3.2 The main principle underlying the research component of the Act is that human tissue samples are donated for research – either a specific research study or for generic research. Samples are not donated to an individual, organisation or institution. This means that individuals, organisations and institutions are not free to do whatever they like with the samples and they do not legally own the samples.

3.3 The establishment of the Human Tissue Authority (the “HTA”) was set out in the Act. The HTA is responsible for overseeing implementation of the Act and was tasked with producing a set of Codes of Practice. In particular, Code of Practice 9 relates to the use of human tissue in research.

3.4 Research involving gametes and embryos is governed by the Human Fertilisation and Embryo Acts 1990 as amended in 2007.

3.5 There are separate regulations where cellular material derived from human tissue may be used for therapeutic purposes (the Human Tissue (Quality and Safety) Regulations 2007).

3.6 Relevant Material

3.6.1 The Act is concerned with regulating activity involving Relevant Material. This is defined as “… any material, other than gametes, which consists of, or contains, human cells.”

3.6.2 Embryos outside the human body, hair, nail and extracted DNA are not Relevant Material. But they are included in an expanded definition of Bodily Material.

3.6.3 Blood plasma, serum and urine may contain human cells and are considered Relevant Material until it is processed to make it acellular and the residual cellular material has been discarded.
3.6.4 A cultured human cell line is Relevant Material for as long as it is likely still to contain original cells from the person who donated them. Once the cell line has been established and is unlikely to contain original cells, then it is no longer regarded as Relevant Material.

3.6.5 The Act also covers activity that involves extraction of DNA from Bodily Material (which includes all Relevant Material plus embryos, hair and nail).

3.7 The main issues to consider for research involving human tissue are:

3.7.1 Consent to collect, use and store tissue samples for research;

3.7.2 Licensing to store the samples; and

3.7.3 Research ethics review of research to use the samples.

3.8 The Act applies differently depending on whether tissue samples are collected and used for a specific research study or for generic research.

3.9 **Tissue collection (Consent)**

3.9.1 Subject to the exceptions below, there must be explicit consent to collect human tissue for research.

3.9.2 Tissue may be collected for storage and use in research without consent provided:

   (a) It is not reasonably likely that the researcher using the samples would be able to identify the person from whom the samples were taken;

   (b) The specific research study for which the samples are to be used has been approved by an NHS Research Ethics Committee (or is covered by the ethics approval for an HTA-licensed tissue bank); and

   (c) The person from whom the samples were taken was alive at the time the samples were taken.

3.9.3 Imported material is not subject to the consent provisions of the Act, but it is regarded as good practice for there to be mechanisms in place to provide assurance that the tissue has been obtained with valid consent.
3.9.4 Notwithstanding points 3.9.2 and 3.9.3 above, a key principle of the Act is that, wherever possible, there should be consent to collect samples to use for research.

3.9.5 Consent to collect samples for a specific research study should be obtained using a study-specific information sheet and consent form that has been approved by an NHS Research Ethics Committee as part of the overall review of the research study. An alternative is possible for samples collected under the auspices of the University of Birmingham’s Human Biomaterials Resource Centre (HBRC) in which case the Trust’s standard “Consent to Examination or Treatment” form may be used (see section 3.10).

3.9.6 If it is likely that some tissue samples may remain at the end of the initial research study and it is intended that these could be used for further research, then the initial consent form should include an option to use samples for future ethically approved, unspecified research. Otherwise re-consent will be required to use the samples for another study.

3.10 Surgical Consent Form

3.10.1 Residual human tissue, generated from a surgical procedure, or taken for diagnostic purposes which would otherwise be discarded, may be used for research provided there is explicit consent from the patient.

3.10.2 For this purpose the Trust’s standard “Consent to Examination or Treatment”, often referred to as the Surgical Consent Form, contains an option for patients to consent to the use of discarded tissue for generic research.

3.10.3 The Surgical Consent Form can be used only to collect residual tissue after an appropriate surgical procedure or collection of blood samples for diagnosis.

3.10.4 The Surgical Consent Form should not be used to collect samples for a specific research project unless this process has been approved by an NHS Research Ethics Committee or the samples are collected under arrangements covered by the ethics approval for an HTA-licensed Human Tissue Bank.

3.10.5 Except for samples collected under the auspices of the HBRC, the standard Surgical Consent Form should not be used if additional samples are needed during a standard procedure or if an additional procedure is required specifically to obtain tissue samples for research. In these circumstances an ethically approved, study-specific information sheet and consent form must be used.
3.10.6 The discussion with the patient about collecting, storing and using the tissue samples for research must be recorded in the patient’s medical records.

3.10.7 Consent from relatives or legal representatives is always required to take relevant material from the deceased for research purposes (see section 3.21).

3.11 **Tissue collection from surgical theatres**

3.11.1 If some tissue samples are required for diagnostic purposes and some for research, then the portion taken for research must not compromise the diagnostic utility of the remaining sample.

3.11.2 For this reason, a portion of a diagnostic sample may only be taken for research when approved by a pathologist or it is taken under the auspices of the HBRC.

3.11.3 The Trust’s Pathology Laboratory will maintain a log of samples released for research. Samples may be retrieved for a specific study or by staff from the HBRC.

3.11.4 Samples can only be taken from Surgical Theatres if

(a) Prior notification of the request has been agreed with the lead surgeon; and

(b) A written record is completed detailing the removal of the tissue sample.

3.12 **Existing Samples**

3.12.1 It is permissible to use existing samples stored in an NHS diagnostic laboratory without consent provided that:

(a) It is not possible for the researcher using the samples to be able to identify the person from whom the samples were taken;

(b) The specific research study for which the samples are to be used has been approved by an NHS Research Ethics Committee (or is covered by the ethics approval for an HTA-licensed tissue bank); and

(c) The person from whom the samples were taken was alive at the time the samples were taken.
3.12.2 HBRC staff are able to collect samples from Trust laboratories for studies approved by the HBRC review committee that fall within the scope of the NHS ethics favourable opinion for the HBRC.

3.12.3 Samples collected specifically for research cannot be stored in NHS or University diagnostic laboratories unless the laboratories are covered by an HTA research licence.

3.12.4 Diagnostic laboratories cannot advertise themselves as a resource for researchers unless they hold an HTA research licence.

3.12.5 None of the diagnostic laboratories in the Trust or at the University of Birmingham currently (April 2015) hold HTA research licenses so they are not able to hold Relevant Material collected for generic research, nor may they advertise themselves as a resource for researchers.

3.13 Traceability of Samples

3.13.1 A formal written record must be made by Theatre or laboratory staff for each and every tissue sample taken for research purposes. This is to make it possible to trace samples if there is ever a request from a tissue donor to know how the samples were used, and to enable auditing for compliance with the regulations.

3.13.2 For samples collected from Theatres, Pathology or Clinical Immunology, the record should include:

(a) Unique id reference for the sample

(b) Location from where sample was collected (e.g. which surgical theatre)

(c) Patient’s NHS number

(d) Trust’s research study reference number (so-called RRK-number) or HBRC study reference number if the sample was collected for an HBRC approved study

(e) Identify of the person collecting the sample

(f) Date and Time of collection

(g) Confirmation that patient consent to donate the tissue was given
(h) Name and signature of the person collecting the sample

3.13.3 A copy of the record for samples collected from Theatres must be sent by theatre staff to Pathology which will maintain a central record store.

3.13.4 The person collecting the sample should be given only the unique id reference for the sample to ensure anonymity of the donors.

3.13.5 For samples collected directly by researchers for a specific research study then a log must be maintained on the Study Site File.

3.13.6 Researchers must keep a record of storage, use and disposal of samples.

3.13.7 This record should include:

(a) Tissue sample ID

(b) Trust’s study reference number (RRK-number), or HBRC study reference number if the sample was collected for an HBRC approved study

(c) Exact location (institution, building, room, cupboard/fridge/freezer)

(d) Date sample stored

(e) Date sample used

(f) Date sample destroyed or if sent to a different organisation, the date the sample was sent and the contact details of the recipient

3.13.8 The samples themselves should be appropriately labelled with the sample id and study reference, but should not contain information that could directly identify the donor (such as name, NHS number or hospital number).

3.14 Existing Holdings

3.14.1 The Act defines Existing Holdings as Relevant Material that was obtained before the Act came into effect (September 2006).

3.14.2 The consent provisions of the Human Tissue Act do not apply retrospectively. This means that it is not a legal requirement to
obtain consent to store or use for research samples that were collected prior to the Act coming into effect. Approval from an NHS Research Ethics Committee is still required though for samples collected prior to September 2006.

3.14.3 However, the HTA recommends that “If practical, the consent of the participant should be sought and the views of the deceased person or of their family (if known) must be respected”.

3.15 Storage (licencing)

3.15.1 Subject to the exception below, Relevant Material collected for research purposes must be stored in premises that are licensed for research by the Human Tissue Authority.

3.15.2 The exception is for Relevant Material collected for a specific research study approved by an NHS Research Ethics Committee which may be stored in any appropriate facility for the duration of the study.

3.15.3 There are no specific storage requirements for samples that are not considered Relevant Material, although material that requires processing to make acellular for non-specific research can only be stored for a maximum of 7 days outside a licensed facility.

3.15.4 Licensed facilities are subject to inspection by the Human Tissue Authority and must comply with quality standards issued by the HTA.

3.15.5 It is expected that unlicensed facilities holding samples for specific studies approved by an NHS Research Ethics Committee should follow some basic quality standards. These include:

(a) Temperature controlled (and preferably monitored) fridges and freezers

(b) Protection of samples from contamination

(c) Adequate labelling of samples

(d) Appropriate documentation

(e) Appropriate security measures

(f) Back-up procedures in case of emergency (e.g. power loss etc.)
3.15.6 Although samples collected for diagnostic purposes and stored in the Trust’s pathology labs may be used for research, it is not possible to collect samples specifically for research and store them in the pathology labs because they do not hold an appropriate HTA licence for research (see 3.12.3 - 3.12.5).

3.15.7 An unlicensed laboratory holding relevant material for diagnostic purposes may not advertise itself as a research resource, otherwise this would be deemed as a research collection and require licensing with the HTA.

3.16 **Temporary Storage (pending processing or transport)**

3.16.1 Samples containing cellular material that are intended to be processed to make acellular (and therefore not subject to licensing requirements) or will be sent to another organisation, may be held for a short period in an unlicensed facility.

3.16.2 The HTA Code of Practice specifies this period as no more than 1 week. After that, the samples must be transferred to a licensed facility.

3.16.3 Similarly, samples that are intended to be transferred to a licensed tissue bank may be stored for no longer than a week in an unlicensed facility.

3.17 **Use (ethics)**

3.17.1 Any research study that wishes to use Relevant Material for research (including material that will be processed to make acellular) must be approved by an NHS Research Ethics Committee.

3.17.2 The ethics review process will check the arrangements for consent, storage and use of samples.

3.17.3 Any change in the way samples will be collected, stored or used during the study must be notified to the ethics committee as an amendment.

3.17.4 Tissue samples collected for use for one research study may not be used for a different study unless the alternate study has received a favourable opinion from an NHS Research Ethics Committee and there is explicit consent from the donor for use of the samples in the new study or for generic research.

3.17.5 An HTA-licensed Tissue Bank may apply for a special form of review by an NHS Research Ethics Committee. Following a
favourable opinion by the ethics committee, the Tissue Bank is given delegated authority to carry out ethical and scientific reviews on behalf of the main NHS Research Ethics Committee of studies proposing to use samples held by the bank: separate review by an NHS Research Ethics Committee is not required for these studies.

3.17.6 The Tissue Bank must provide an annual report to the main NHS Research Ethics Committee of all studies approved to access the facility (see section 3.20).

3.18 **Non-consensual DNA analysis**

3.18.1 It is a criminal offence to hold tissue samples with the intention of performing DNA analysis without consent unless:

(a) The material was collected before 2006 and it is not possible for the researcher to identify the person from whom the sample came; or

(b) The material comes from a living person and

(i) It is unlikely that the researcher would come into possession of information to identify the person from who the material came; and

(ii) It is for a specific research study that has been approved by an NHS Research Ethics Committee.

3.19 **End of Study**

3.19.1 If there are any samples remaining after the declaration of the end of a research study then they must either:

(a) Be destroyed

(b) Transferred back to the original NHS diagnostic laboratory if they remain of diagnostic value

(c) Transferred to an HTA Licensed Tissue Bank

(d) Formally transferred onto another research study that has a Favourable Opinion from an NHS Research Ethics Committee

3.19.2 Samples cannot be held pending a future application for favourable opinion from an NHS Research Ethics Committee

3.20 **Licenced Tissue Banks**
3.20.1 An important function of the Act was to establish a framework for promoting storage of collections of tissue samples for wider use in research.

3.20.2 The collections are held under research storage licenses issue by the Human Tissue Authority.

3.20.3 These collections are available to anyone wishing to use them for high quality research through a formal application process controlled by the Tissue Bank administrator.

3.20.4 In Birmingham the main tissue bank is the Human Biomaterials Resource Centre (HBRC).

3.20.5 Applications to use samples are assessed by a scientific and ethical review committee. The samples cannot be held or reserved for specific researchers.

3.20.6 All samples must be released anonymised or link-anonymised (i.e. samples are labelled with a code so that although they are anonymised for the researcher, administrators at the tissue bank retain the key to be able to re-identify the source of the samples if further clinical information is required). Researchers must not make any attempt to try to identify the person from whom a sample is taken (particularly if samples relate to a rare disease or treatment).

3.20.7 HBRC staff can retrieve and pass on associated clinical data from patient medical records linked to the samples.

3.20.8 An annual summary of researcher studies accessing samples held in the Tissue Bank must be submitted to the main ethics committee.

3.20.9 **HBRC Retrieval Service**

(a) Staff employed by the HBRC are able to provide a service to retrieve anonymised tissue samples from surgical theatres or NHS diagnostic laboratories for specific research studies. These studies may be covered either by the Tissue Bank Ethical approval or by a study-specific ethical approval.

(b) This service is not appropriate if any additional procedures are required for the study (e.g. additional imaging or patient visits), or if non-routine clinical data is required, in which case the study should be submitted as a full application to an NHS Research Ethics Committee.
3.20.10 **HBRC Hosting Service**

(a) The HBRC provides a hosting service to store samples in HTA-compliant facilities for specific research studies.

(b) These samples are stored for a specific study and access is controlled by the Chief Investigator of the study.

(c) The samples do not come within the HTA research licence of the tissue bank or the Ethical approval for the bank.

(d) At the end of the research study any residual samples must be destroyed, transferred into the HTA-compliant tissue bank’s licensed collection or formally transferred into another specific study that has a Favourable Opinion from an NHS Research Ethics Committee.

(e) The HBRC applies a fee for use of the hosting service.

### 3.21 Deceased

3.21.1 Some additional specific rules apply to tissue samples taken from the deceased (see also section 3.22).

3.21.2 Appropriate consent from a relative or legal representative **must** be obtained to collect and use tissue samples from the deceased for the purpose of research, even if the samples are anonymised.

3.21.3 **Removal** of tissue sample from the deceased with the specific intention of using it for research can only be done in a facility that is licensed by the Human Tissue Authority (so-called ‘Removals’ licence)

3.21.4 In this Trust the Pathology Laboratory is the only facility licensed to remove tissue from the deceased: **tissue intended for research cannot be removed from the deceased in the surgical theatres.**

### 3.22 Transplantation
3.22.1 Tissue that has been removed from a deceased person for the purposes of transplantation but proves not to be suitable, may be used for research provided there is consent from the relatives or legal representative, or the source of the tissue is not identifiable by the researcher and it is to be used in a research study approved by an NHS Research Ethics Committee.

3.22.2 Studies that are likely to involve the Organ Donation and Transplant (ODT) services of NHS Blood and Tissue (NHSBT), for example if retrieval involves Speciality Nurses in Organ Donation (SNODs), must be registered and approved by NHSBT.

3.22.3 It is permitted to use discarded samples that are generated as part of the process of preparing an organ for transplantation provided there is appropriate consent from a relative or legal representative.

3.22.4 Unless the facility is covered by a Removals Licence, it is not permitted to take additional samples while removing an organ. There must always be appropriate consent to do this.

3.23 Advanced Therapies

3.23.1 There are separate regulations where cellular material derived from human tissue may be used for therapeutic purposes (the Human Tissue (Quality and Safety) Regulations 2007).

3.23.2 The procurement, testing, processing, distribution, import or export of cells for therapeutic purposes are all licensable activities regulated by the Human Tissue Authority.

3.23.3 A licensable activity may be carried out in an unlicensed facility provided there is a third party agreement between the licensed establishment and the other organisation. This particularly applies where tissue procurement is carried out in NHS hospitals for processing elsewhere.

3.23.4 A third party agreement is also required if an unlicensed establishment is providing goods or services that might affect the quality of the product.

3.23.5 The HTA must be given prior notification of the intended use of a third party establishment and the HTA has the authority to inspect any third party establishment.

3.23.6 There must be a documented system in place that ensures that every unit of tissue or cells can be identified at all stages from procurement through to end use (procurement, testing,
3.23.7 The processed cells are usually regarded as Advanced Therapy Medicinal Products (ATMPs) so also come under the Clinical Trials Regulations (Statutory Instrument 2004:1031 Medicines for Human Use (Clinical Trials) Regulations 2004).

3.23.8 A consequence is that the processing establishment must hold a manufacturing licence with the Medicines and Healthcare Products Regulatory Agency (MHRA).

4 Duties

4.1 Head of Research and Development (R&D) Governance

4.1.1 Reviews the proposed collection, storage and use of human tissue samples in research studies

4.1.2 Oversees audits of active studies which includes assessment of collection and storage of human tissue samples

4.2 Head of HBRC

4.2.1 Manages the process for collecting tissue samples for studies reviewed under the HBRC’s NHS Research Ethics Committee favourable opinion.

4.2.2 Maintains a record of all tissue samples collected under the auspices of the HBRC

4.2.3 Provides an annual report to the NHS Research Ethics Committee, copied to the Trust, summarising collection and storage of tissue samples in the HBRC

4.3 Head of Tissue Services

4.3.1 Oversees arrangements to ensure compliance with HTA-requirements for procurement of tissue samples for therapeutic purposes

4.4 Designated Individual, HTA Post Mortem Licence

4.4.1 Ensures that tissue samples are only taken from pathology laboratories for studies that have been approved by the Trust’s R&D Governance Office

4.4.2 Ensures that a record is kept of all requests for tissue samples. This record should be available for review by the Head of R&D Governance
4.5 **Surgical Theatre Managers**

4.5.1 Ensures that only tissue samples are only taken for research studies that have been approved by the Trust’s R&D Governance Office, or by the HBRC review panel. Ensure that a record is kept of all tissue samples collected for research purposes and that a copy of the record is sent to the Head of Pathology services.

5 **Implementation and Monitoring**

5.1 Review of tissue handling arrangements is included as part of the standard R&D Governance Office process for assessing research study applications.

5.2 The University of Birmingham Human Biomaterial Resource Centre has an extensive set of operating procedures.

5.3 New standard procedures will be developed for tracking requests for tissue samples from surgical theatres and Trust pathology laboratories.

5.4 Researchers are required to complete and return annual progress reports to the R&D Governance Office. These reports are in a standard format and include questions about the collection, storage and use of tissue samples.

5.5 The R&D Governance Office has a schedule of random audits of research studies in the Trust. Part of the audit includes a review of the arrangements for handling tissue samples. A summary of audit findings is presented at each meeting of the R&D Management Group and annually to the Trust’s Audit Committee.

5.6 The HBRC produces an Annual Report for the National Research Ethics Service which gives details of all studies approved by the HBRC. A copy is supplied to the Trust together with a breakdown of requests for samples from the Trust.

6 **References**

6.1 Human Tissue Act 2004


6.3 Statutory Instrument 2004:1031 Medicines for Human Use (Clinical Trials) Regulations 2004

6.4 Human Tissue Authority Code of Practice 9 – Research (September 2009)
## Appendix 1

**HTA Licences held by University Hospitals Birmingham and the University of Birmingham (April 2015)**

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<th>Licenced Establishment</th>
<th>Designated Individual</th>
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<tr>
<td><strong>Research</strong></td>
<td>University of Birmingham School of Dentistry</td>
<td>Iain Chapple</td>
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<tr>
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<td>University of Birmingham Medical School (HBRC)</td>
<td>Jon Frampton</td>
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<tr>
<td><strong>Post Mortem</strong></td>
<td>Queen Elizabeth Hospital Birmingham</td>
<td>Rachel Brown</td>
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<tr>
<td><strong>Tissue and Cells</strong></td>
<td>Birmingham and Midland Eye Centre (distribution, export and storage only)</td>
<td>Adam Slater</td>
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<tr>
<td></td>
<td>Queen Elizabeth Hospital Birmingham (distribution, export, procurement, storage and testing)</td>
<td>Julie Dulson</td>
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<td><strong>Organ Donation and Transplant</strong></td>
<td>Queen Elizabeth Hospital Birmingham</td>
<td>Julie Moore</td>
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