Imperial College Healthcare NHS Trust

Imperial College London

**IMPERIAL COLLEGE HEALTHCARE TISSUE & BIOBANK: PROJECT DESCRIPTION**

Imperial College Healthcare Tissue & Biobank is an umbrella structure that is responsible for collecting and storing biological samples from a variety of different sources at Imperial College London and its sister organization Imperial College Healthcare NHS Trust as well as the Chelsea and Westminster Hospital NHS Trust and the London North West Healthcare NHS Trust. The ICHTB ensures that biological samples are used for approved research projects in a manner that is consistent with the consent obtained. The general structure of ICHTB and its governance is given in Section A. This is a complex project that combines a number of different consent procedures under one Research Ethics approval. It is most logical to divide this into different groups of donors, each of which shares a common consent mechanism. These are outlined in section B below.

Biological samples are only useful for research if they are annotated with information. Section C in this project description provides information on how information from the NHS clinical record is linked to samples stored under ICHTB's umbrella, and how this data is pseudonymised to protect the donor's identity.

In addition to collecting biological samples, ICHTB is also responsible for approving research projects that use these samples. The mechanism by which this is done is described in Section D.

ICHTB works closely with Imperial Joint Research Compliance Office to ensure that all human research carried out on our campuses is carried out within the relevant regulatory guidelines.



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# Section A – Structure of ICHTB and Governance.

## A.1 Organisational Structure of ICHTB

The main tissue collection comprises material from operative specimens that is surplus to diagnostic requirement. However, many of our clinicians also wish to collect fluid samples (e.g. blood and urine) from their patients to provide banks of material for future use in research projects. ICHTB therefore also provides a mechanism whereby local Principal Investigators can collect and store biological samples from patients under their care. Information on who is storing what and in which location is entered into a centralized database that provides local PIs with a tracking system to record the movement of samples in and out of their collection and to upload files relevant to their subcollection e.g. SOPs for collection, annotation, etc. (for further information see Section C). There are different types of sub-collections that are held under the HTA Licence at Imperial. With regard to this application, subcollections in the first group are the most relevant with respect to consent of the donors. However as there is the potential for all three groups of subcollection to be approved for research use via the application for access procedure (see section D) for which we also seek HRA approval. Broadly these subcollections can be divided into 3 categories.

## A.2 Subcollection categories

### A.2.1 Donors consented using ICHTB approved consent material

The majority of our subcollections are those which use Tissue Bank consent material(s) – listed in section B - are used to consent donors and materials are stored on ICHT/ICL premises. Further information is given in Section B.

Subcollection registration (see section A.2.4 below) enables PIs to collect and store material but not to use material from their collection. To use material for research they must, in addition, register a separate project that must be approved by a subgroup of the Tissue Management Committee (TMC: see section A.3.2). Multiple different projects can be issued samples from each subcollection, but each project must be approved via the mechanism set out in Section D.

### A.2.2 Donors consented using separate specific HRA approved consent material (i.e. not part of this current REC approval)

These are subcollections where alternative consent materials, not included in this application, are used to consent donors and consent is on-going from donors in our Trust or College. These must have separate HRA approval and PIs must provide a copy of the consent form/PIS and a copy of their HRA approval letter. PIs must also provide amendments to the REC approval when made. Some of these will have agreed use of some or all of their samples within their specific HRA approval. In this case we do not need to have the specified use of samples approved by TMC as they are covered by the original HRA approval. If the samples are to be used for other studies that have not been stated under the original HRA approval, the PI must seek an amendment when the subcollection remains within the HRA approval dates. At the end of accrual of samples and HRA approval the PI can either seek renewal of specific HRA approval for their project or, where there is an element of generic consent for future unspecified use, place the samples under the HTA Licence as part of ICHTB. In the latter case any further use of samples must go through TMC approval (see section D).

## A.2.3 "Imported" Sub-collection

These are sub-collections where the material is imported into ICL/ICHT from other institutions including those from outside the UK. These are similar to (A2.2) above but will not necessarily have UK HRA approval. If they do not have UK HRA approval (i.e. they are imported from abroad), the PI must provide a document that states that the samples have been sourced in accordance with the local rules with regard to ethics and law. These can also be collections of clinical trial materials, initially stored outside Imperial, where the original HRA approval has lapsed, but generic consent for research use of material was sought. All subcollections must have a Material Transfer Agreement (MTA) that specifies where the samples have come from, and what they can be used for. Where the material has been consented using HRA approved forms a blank copy of the consent form and patient information leaflet must be provided. If the subcollection has been established for use only within what is agreed on the MTA, approval for use is not required via the TMC, providing the information on the MTA is very specific and that any residual material is to be destroyed following completion of that specific project. Where future undefined research is to be carried out, and this has been agreed by the supplier of the material, each project must go through TMC approval (see section D).

On registration, all sub-collections are given a code that links them to the Department of the PI, and to the PI themselves.

## A.2.4 Roles and Responsibilities of PIs of subcollections

Each subcollection must have a nominated PI who is responsible for ensuring that the subcollection is appropriately managed and who provides regular reports to the Designated Individual (DI) for the HTA Licence, through the Person Designate on their campus who has been allocated the responsibility for oversight of their subcollection. These role and responsibilities are set out in Annex 1. The PI must register the subcollection on the Tissue Bank database – is done using an online system that allows the PIs to input the data directly into the database. Applicant are provided information regarding this procedure in a Guide to registering a sub-collection under the HTA Licence (see TB-SOP-005SCM in Annex 1). PIs are expected to provide the following documents or to agree to abide by the SOPs provided by Tissue Bank staff that govern these elements when samples are received via Pathology for material left over from operations:

- procedure for obtaining and documenting donor consent and receipt of samples
- procedure for disposal of samples
- procedure for transport of samples (into storage and from storage)
- procedure for cleaning and decontamination
- procedure for managing abnormal changes in storage temperatures
- procedure for recording and reporting adverse events to the DI

Where the subcollection does fall into the type described in A2.2, the PI is also obliged to provide a blank copy of the consent form and patient information leaflet, and a copy of the Ethics approval for the sample collection and use. Where material has been provided from abroad a document with a statement that the material has been obtained according to the local ethics and law of the country in which the samples were sourced must also be provided. All externally sourced samples must have an MTA that details the samples brought in and the use that has been agreed by the supplier.

The Tissue Bank database provides an online tracking facility to check samples in and out of the subcollection, but in some cases where large legacy collections have been imported and already have a tracking database, PIs may prefer to continue to use their own system. Where this is the case, there must be a statement to this effect provided to the Tissue Bank together with details on who has access to the

database and could be asked to assist with any audits that may be required for the HTA Licence. PIs are responsible for providing an annual report on the number of samples accrued and used (see Annex 1) for both HRA and HTA reporting purposes. PIs are permitted to nominate a deputy to carry out these tasks.

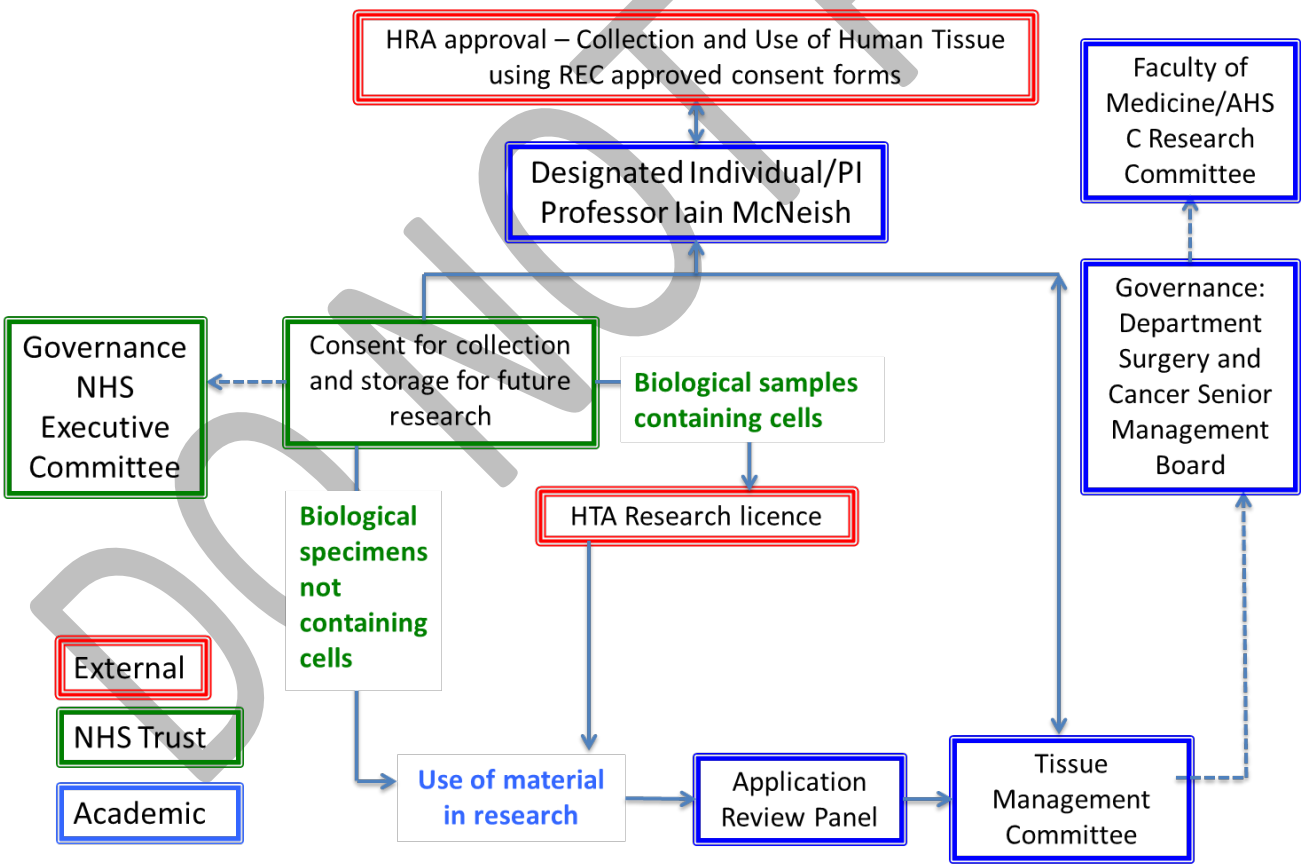
Any applications for access to a subcollection must be approved by the PI of that subcollection (see section D for details).

When a PI leaves employment at the College or the Trust they must nominate a current employee to take on their role, but where they retain an honorary contract they still retain rights over access to the material. PIs may seek to take their collections with them to their new employer, but this can only be done with the consent of their Head of Department at Imperial and assurances must be provided by the new Institute that the material transferred can be stored appropriately. Removal of samples must be subject to an MTA stating what use can be made of the samples to ensure that the consent provided by the patient is respected.

## A.3 Governance of ICHTB

The Governance structure for ICHTB is given in Figure 1. Governance can be divided into 2 areas – tissue collection and use of tissue in research.

Figure 1 – ICHTB Governance



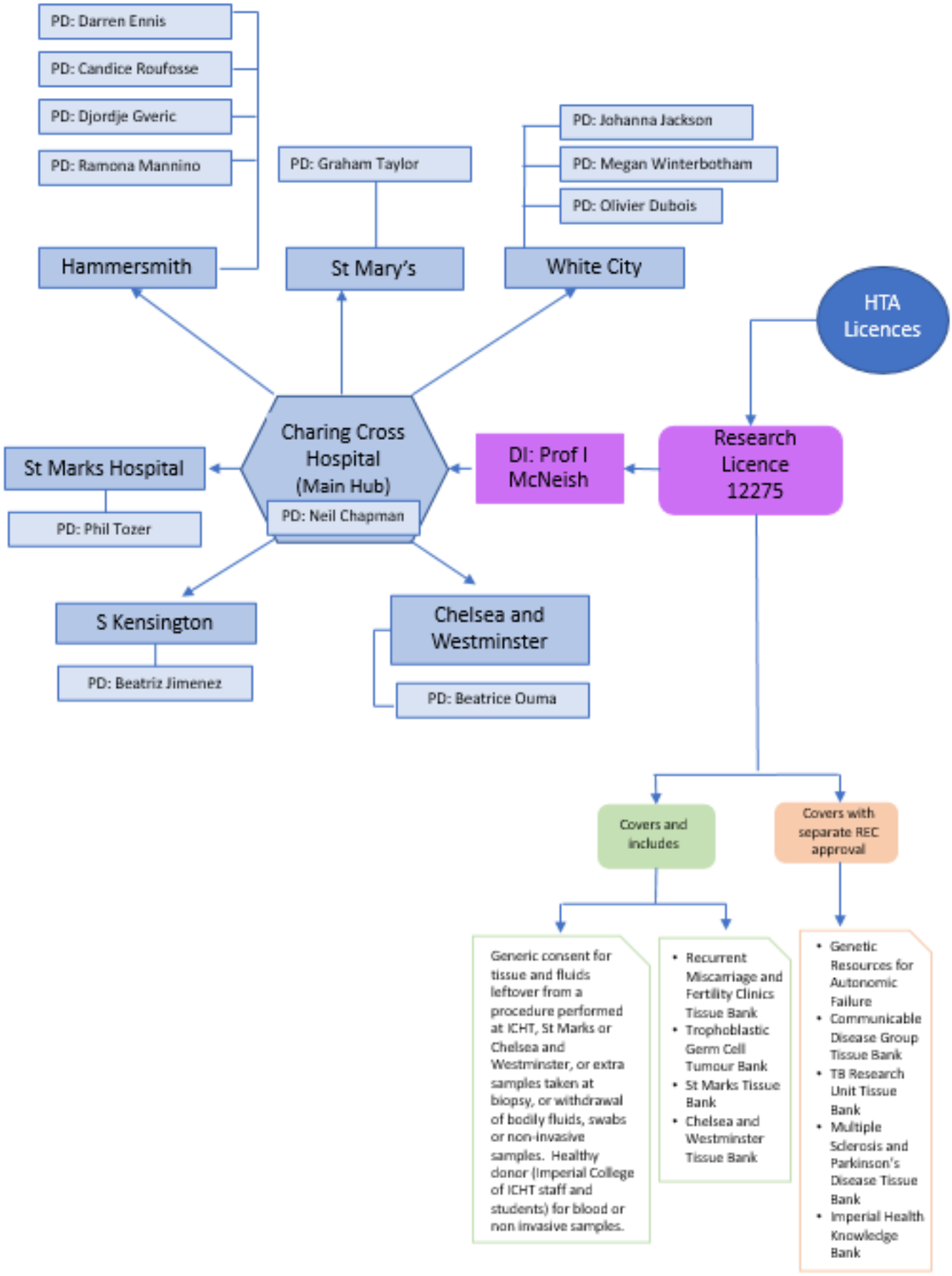

## A.3.1 Tissue Collection

The Tissue Bank staff comprises a Tissue bank Manager, a Sub-collection Manager, who is responsible for general management of sub-collections and audit, a Senior Technician responsible for the management of

the Tissue Bank laboratory and 4 other technical staff. ICHTB has 3 collection sites for human material from Imperial College Healthcare NHS Trust patients undergoing operations: Hammersmith, Charing Cross and St Mary's Hospital, all of which form Imperial College NHS Trust. The Tissue Bank office and laboratory is at Charing Cross Hospital. The Recurrent Miscarriage Tissue Bank is based at St Mary's Hospital and is run by Professor Lesley Regan as part of her clinical practice. The Trophoblastic and Germ Cell Tumour Bank is run by Geoffrey Maher as part of his clinical practice at Charing Cross Hospital.

In addition to patients consented through ICHT, Imperial College academics hold contracts with two other NHS Trusts – London Northwest University Healthcare NHS Trust (LNUHT) and Chelsea and Westminster Healthcare NHS Foundation Trust (C&WT). These academics are closely associated with two hospital sites – St Marks Hospital, which is located on the Northwick Park campus of LNUHT and the Chelsea campus of C&WT. The HTA has approved these two sites as satellites to the HTA Research Licence. On both of these satellites, collection of patient samples is limited to a few specialized teams. These collections are held as sub-collections under the HTA Licence, but require separate Trust specific consent materials to be provided to patients. These can be found in Annexes 12 and 13 to this application. The consent materials have been designed to mirror the ICHT consent materials as closely as possible.

Charing Cross is the hub for the HTA Licence and Hammersmith, St Marks Hospital on the Northwick Park Campus, St Mary's Hospitals and Chelsea and Westminster are listed as satellite sites.
As some human material is stored at Imperial's central non-clinical site, South Kensington and White city Campuses are also listed as satellite site under the HTA Licence. Each of our collection sites has a number of Persons Designate who are responsible for day to day supervision of activity on their site, and provision of local advice to researchers (see Figure 2). Patient information sheets and consent forms have been NHS Trust approved, and the Sub-collection manager works with the clinical teams on each site to ensure that consent is taken appropriately. Standard Operating Procedures for taking consent are available on the Tissue Bank webpages (www.imperial.ac.uk/tissuebank) and are included in the Annexes to this application. The Tissue Bank technicians check that consent is in place prior to taking samples for research (see section B.1 below). Consent forms are subject to regular rolling audit. The clinical teams that collect material for subcollections are responsible for obtaining consent from their donors, and this is also subject to regular rolling audit by the Sub-collection manager. Annual reports are provided to the ICHT Research Committee and include information on consent issues. Annual reports are also provided to the Senior Management Committee of the Department of Surgery and Cancer, the host Department for the current Designated Individual for the HTA Licence.


PD: Darren Ennis
PD: Candice Roufosse
PD: Djordje Gveric
PD: Ramona Mannino
Hammersmith
PD: Graham Taylor
St Mary's
PD: Johanna Jackson
PD: Megan Winterbotham
PD: Olivier Dubois
White City
HTA Licences
Charing Cross Hospital (Main Hub)
PD: Neil Chapman
St Marks Hospital
PD: Phil Tozer
DI: Prof I McNeish
Research Licence 12275
S Kensington
PD: Beatriz Jimenez
Chelsea and Westminster
PD: Beatrice Ouma
Covers and includes
Covers with separate REC approval
Generic consent for tissue and fluids leftover from a procedure performed at ICHT, St Marks or Chelsea and Westminster, or extra samples taken at biopsy, or withdrawal of bodily fluids, swabs or non-invasive samples. Healthy donor (Imperial College of ICHT staff and students) for blood or non invasive samples.
• Recurrent Miscarriage and Fertility Clinics Tissue Bank
• Trophoblastic Germ Cell Tumour Bank
• St Marks Tissue Bank
• Chelsea and Westminster Tissue Bank
• Genetic Resources for Autonomic Failure
• Communicable Disease Group Tissue Bank
• TB Research Unit Tissue Bank
• Multiple Sclerosis and Parkinson's Disease Tissue Bank
• Imperial Health Knowledge Bank

### A.3.2 Use of Tissue in Research

The Tissue Management Committee (TMC) oversees issues concerning the day to day running of the tissue bank, and the use of material released from it. The TMC meets a minimum of twice a year. Terms of Reference for, and membership of, the Committee are set out in Annex 2. Minutes of the TMC meetings are included in the annual reports to the Trust's Executive Committee and Senior Management Board of the Department of Surgery and Cancer. An Application Review Panel considers applications for use of material taken prospectively with explicit consent (section B below) and material that has been taken exclusively with diagnostic intent, but that may be used for research once the diagnostic process is completed (see section D below). Representatives of the Application Review Panel sit on the TMC and a report of applications and the results of their review is provided to the biannual meetings of the TMC. The HTA has indicated that it is content for stored samples that have been taken for diagnosis and remain after the diagnostic procedure has been completed to be used in research, providing that all samples are pseudonymised to researchers and that there is HRA approval in place, either separately for a specific research project, or that these samples are effectively held within a Research Tissue Bank that has HRA approval for a mechanism of access and "deemed ethics approval" is provided by the Research Tissue Bank mechanism.

## Section B – Consent

A number of different consent mechanisms are included in this application for approval, and these can be broadly divided into 5 groups, listed below.

### B.1 Donors who are patients treated under Imperial College NHS Trust (ICHT)

Diseased tissue is removed from patients during operations as part of their care pathway. Samples from this tissue are taken for diagnostic purposes in the Pathology Department, but in many cases, some material is left over from the original operative specimen. This material is normally disposed of by incineration. This "material" can be extra blocks of fixed tissue taken from the operative specimen, or can be fresh tissue that is subsequently frozen or used for primary culture etc.

Patients are also approached to give fluid samples for diagnosis (e.g. blood, urine, pleural or ascitic fluid). As with material from surgery, sometimes some of the sample remains after the diagnostic procedure, and would normally be disposed of by incineration.

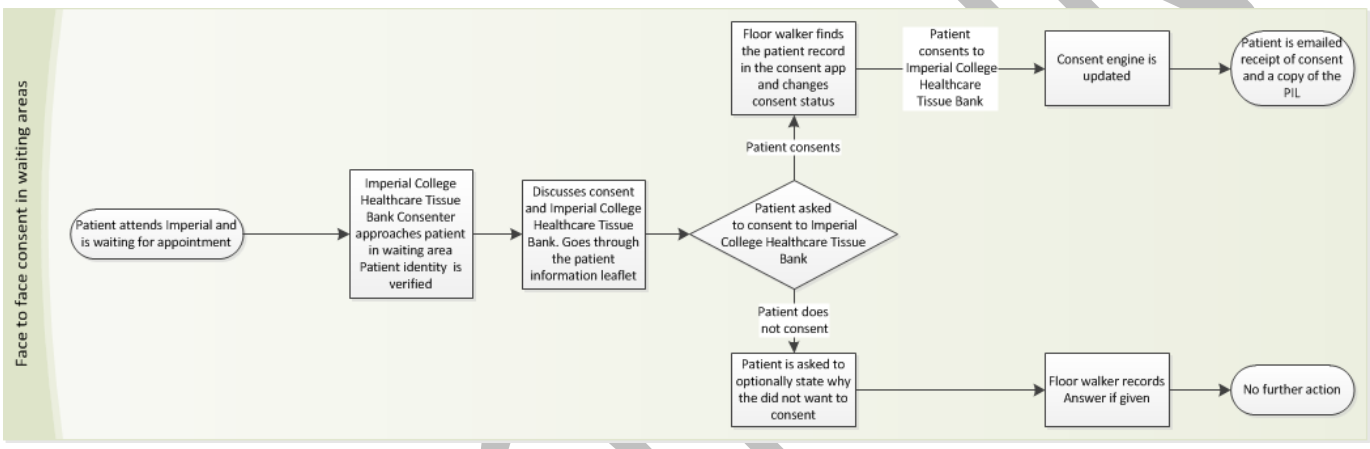
With the patient's permission this leftover material can be used for research purposes.

All aspects of the collection, documentation, further processing and storage of materials are carried out to specific Standard Operating Procedures. All documentation is managed within a Sharepoint document management system, and the ICHTB database provides a Laboratory Information Management System using barcodes to track movement of samples in and out of the tissue bank, and, where appropriate, through different processing steps.

ICHT is implementing a Trust wide policy to consent all patients for research use of biological samples and data. Eventually it is hoped that this will operate as a "consent at door" programme, but for the initial phase patients in the ICHTB programme will be consented either electronically by trained Consenters approaching patients in outpatients and clinic waiting rooms or via paper or electronically by NHS clinicians at the point of consenting patients for clinical procedures (e.g. biopsy or surgery).

In both cases Imperial College Healthcare NHS Trust will ensure that the patient is provided with the ICHTB Patient Information Sheet (included in Annex 3) to ensure that consent is informed.
The roll out of electronic consenting has been established in ICHT with the Concentric digital consent application, an online service, used by both clinicians and patients, which digitises the process of gaining procedural consent. Most interactions are driven by clinicians, but specific screens are designed to inform patients, and patients are given online access to their consent information. The platform uses the Concentric ontology, a structured, validated, and versioned repository of surgical information. It is used by the digital consent application to make a body of knowledge available to clinicians during the consent process, has the structure required to allow machine processing, and includes information written in lay language which is made available to patients. The concentric application for ICHT uses the same Patient Information Sheet (included in Annex 3). Screenshots of the consenting page and resulting generated PDF consent forms are included in Annex 14.

Figure 3: ICHTB Electronic consent pathway and ICHTB consenters

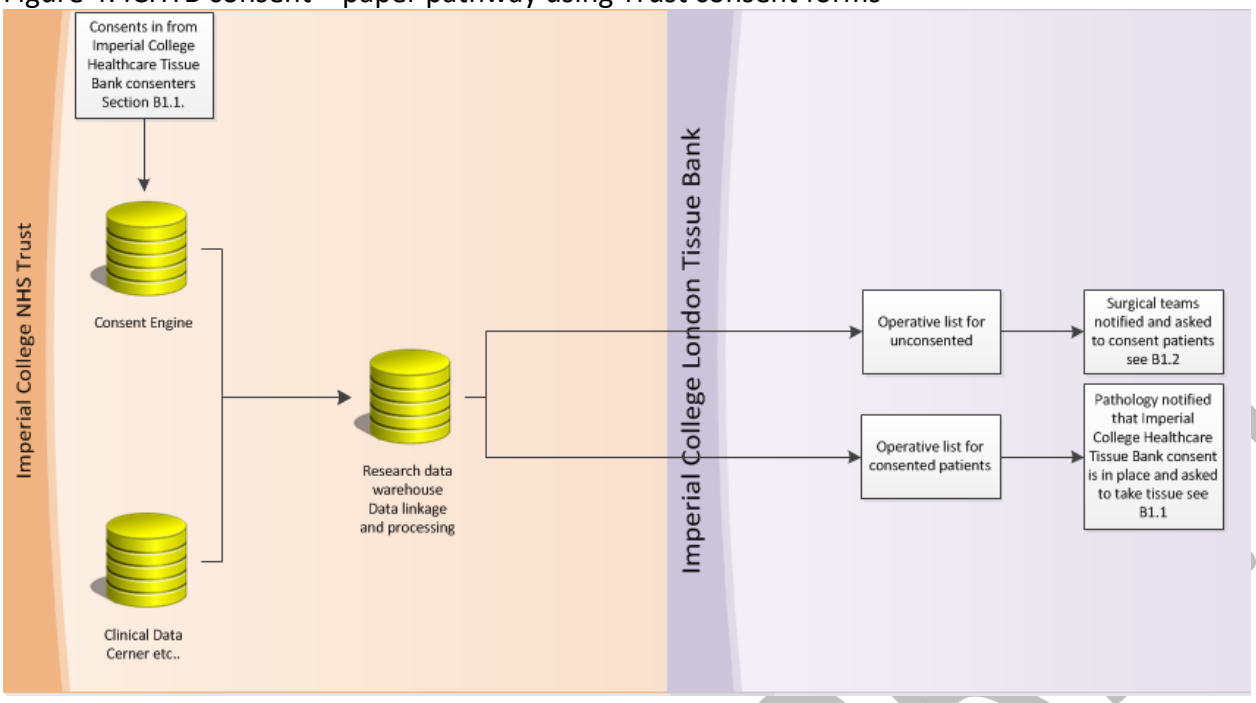



## B.1.2 Consent via clinician/nurse prior to clinical procedure (ICHTB)

Consenting for research is already embedded in the Trust process for consenting a patient to perform a clinical procedure. The current system has been used successfully for a number of years and was approved previously by Wales REC in 2012 and audited by the HTA in 2014. SOPs detailing the procedure, which reflect the proposed use of the ICHTB Patient Information Sheet, are attached as Annexes 3 and 4.

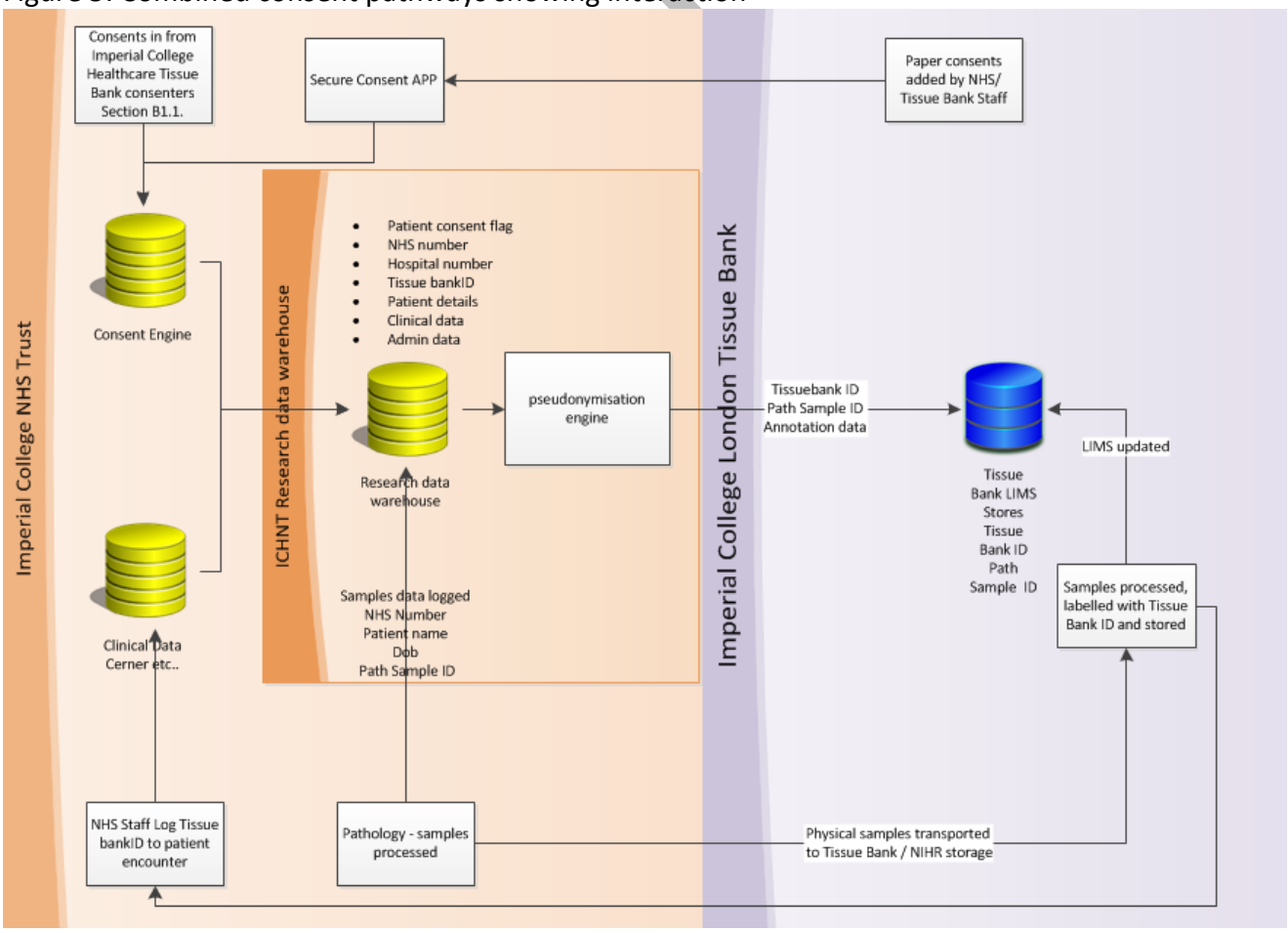
Imperial College Healthcare NHS Trust will move to adapt the consent by clinician or research nurse process to an electronic based system, but this will take time and cannot be replaced in one single step as the process for patient consent to clinical procedures will need to be changed and agreed with the Trust at the same time. Until such time that all consents are registered prior to procedures that would result in biological specimens being taken, the surgical teams will be notified when a patient is booked for an operation when the patient has not already been approached for consent to ICHTB. Each week the research data warehouse will provide Pathology with a list of patients booked for operations the following week who have consented to ICHTB. This will alert Pathology to take a frozen sample of tissue where this does not, in the opinion of the reporting Pathologist, prejudice diagnosis. These samples will then be passed to Tissue Bank staff for further processing and storage. Simultaneously a list of patients who have not yet been approached for ICHTB will be provided to Tissue Bank who will liaise with surgical staff to approach patients for consent to ICHTB at the time of their procedure, using the paper based consent procedure outlined in Annexes 3 and 4 and Figure 4 below.

Figure 4: ICHTB consent – paper pathway using Trust consent forms




When the consent is recorded on a paper form, it will be passed to the Tissue Bank at Imperial College London. NHS staff will then use the Trust consent App to record the consent electronically. Figure 5 shows how the two procedures above will interact.

Figure 5: Combined consent pathways showing interaction



### B.1.2.1 Consent for both invasive and non-invasive samples

Imperial researchers are often involved in projects that seek to develop tests that can be used to diagnose patients using alternative sampling methods – for example, samples of saliva, breath or urine or vaginal, aural, oral or rectal swabs. This usually involves comparisons between samples obtained non-invasively prior to a procedure, during a procedure such as insertion of a rectal or vaginal probe, and an extra tissue sample obtained specifically for research purposes at the time of a biopsy procedure e.g. endoscopy.

Patients who are scheduled to undergo a biopsy procedure and who would be candidates for projects using the approach outlined above will be asked for consent using the "extra samples consent form" when they attend a pre-operative clinic appointment. The person taking consent will seek permission to take non-invasive samples (defined as saliva, sweat, breath, faeces and/or urine) as well as extra biopsy material and document which samples are expected to be provided on the extra sample consent form. Details of this procedure can be found in the SOP for extra sample consent in Annex 4.
Sub cutaneous fat from surgical incisions:

## B.1.3 Recording consent for ICHTB

Imperial have developed a secure consent engine that sits within the clinical systems integration engine within the Trust firewall. The consent engine is maintained within a secure environment with both technical and organisational security measures, only those with a legitimate relationship and subject to the appropriate contractual clauses will have access to the confidential information maintained therein.

The consent engine is designed to manage the multiple consents that are captured in various areas with Imperial and from systems external to Imperial that capture consents that would affect patients' care. The engine is connected to the electronic patient record and has secure interface to Imperial's web interface application to receive consent information from web applications and external systems.
The consent engine allows consents to be actioned appropriately, by interacting automatically with clinical systems to place orders and to inform users of the consent status of patients they are treating.
This consent engine will be used to store and action all ICHTB consents.

As the consent engine is embedded in the Trust electronic patient records system it monitors all phlebotomy orders. When orders for blood samples are sent via NHS clinical staff, the order is checked against the consent engine. If a patient has consented to ICHTB and has not provided a research blood sample, the consent engine will automatically add two blood samples (12.5ml) to the order before it is passed to phlebotomy. Once the patient has provided an initial sample this is logged in the consent engine and no further blood orders are routinely requested for research, unless a specific request is made by an NHS clinician at a later time point in the patients' treatment pathway (e.g. to obtain a blood sample from a cancer patient for analysis of biomarkers that could be used for disease process monitoring).

The consent engine will also be used to provide a unique ID that can be used to link further clinical information on treatment and outcome to biological samples recorded on the ICHTB database (see section C)

## B.1.4 Re-contacting patients

Very occasionally research studies can identify patients that may require a change to the treatment that they are receiving or be suitable for other research studies (e.g. a clinical trial) that may be beneficial to their health. It is important that the patient is made aware of this at the time of consent.

A specific paragraph in the introduction of the PIS states the following "We also want to give you the option to take part in further research studies related to your conditions or that are relevant to you. To do this we need to be able to contact you to provide further details of these studies so you can decide if you want to take part, contact will only be made by NHS clinical staff who will explain the study and ask for your permission to share your contact details with the researcher running the study. You have no obligation to say yes."

The following is also stated explicitly in the PIS:
**"What if you find something new about my health?**
Results for individual patients from particular research studies will not normally be relayed back to you or your doctor. In very rare situations, some research projects could identify changes to your diagnosis or treatment or that may indicate an inherited disease that could affect you or your family members. Your hospital doctor will be notified if any information that is discovered, as a result of the research, may affect you or your family's care."
When and how will I be contacted about research studies that I may wish to participate in?
Approved researchers will be able search your de-identified health data and data obtained from your biological samples to identify people who may be suitable to take part in research studies that assist researchers in improving healthcare and treatments. For example, a search might be conducted to find people who are over the age of 40 and have diabetes.

If your data matches the requirements for a research study that may be beneficial to you, we will allow an NHS clinician at Imperial College NHS Trust to access your contact details to provide you with details of the research study. If you are interested in finding out more, the NHS clinician will pass your contact details on to the researcher who will get in touch with you to discuss it further. You decide if you want to take part. It is your choice and you can say no. Your full identifiable medical record will never be seen.
You do not have to take part in any studies if you do not wish to, and your medical treatment will be unaffected by your decision."
Participation in such future research projects will require separate project specific HRA approval and the patient will be given further information relevant to the project and asked to sign a specific consent form for the project. ICHTB has a specific policy on return of research results to patients – this is included as Annex 5.

In the event of a request from a researcher for recontact, the ICHTB team will be notified of the patients unique tissue bank ID, a NHS clinician will then re-identify the patient via the Trust's consent engine. If the patient is receiving active treatment in the Trust the care team will be contacted and consulted as to whether the patient is suitable for the research study. If the patient is not receiving active treatment then NHC clinician will make an assessment of whether the patient is suitable and contact them with details if they are.

When patients are contacted by phone, they will be asked informed of the details of the study and asked if the want to receive further details. If they want to take part, permission will be sought for the researcher to contact them about enrolling in the study.

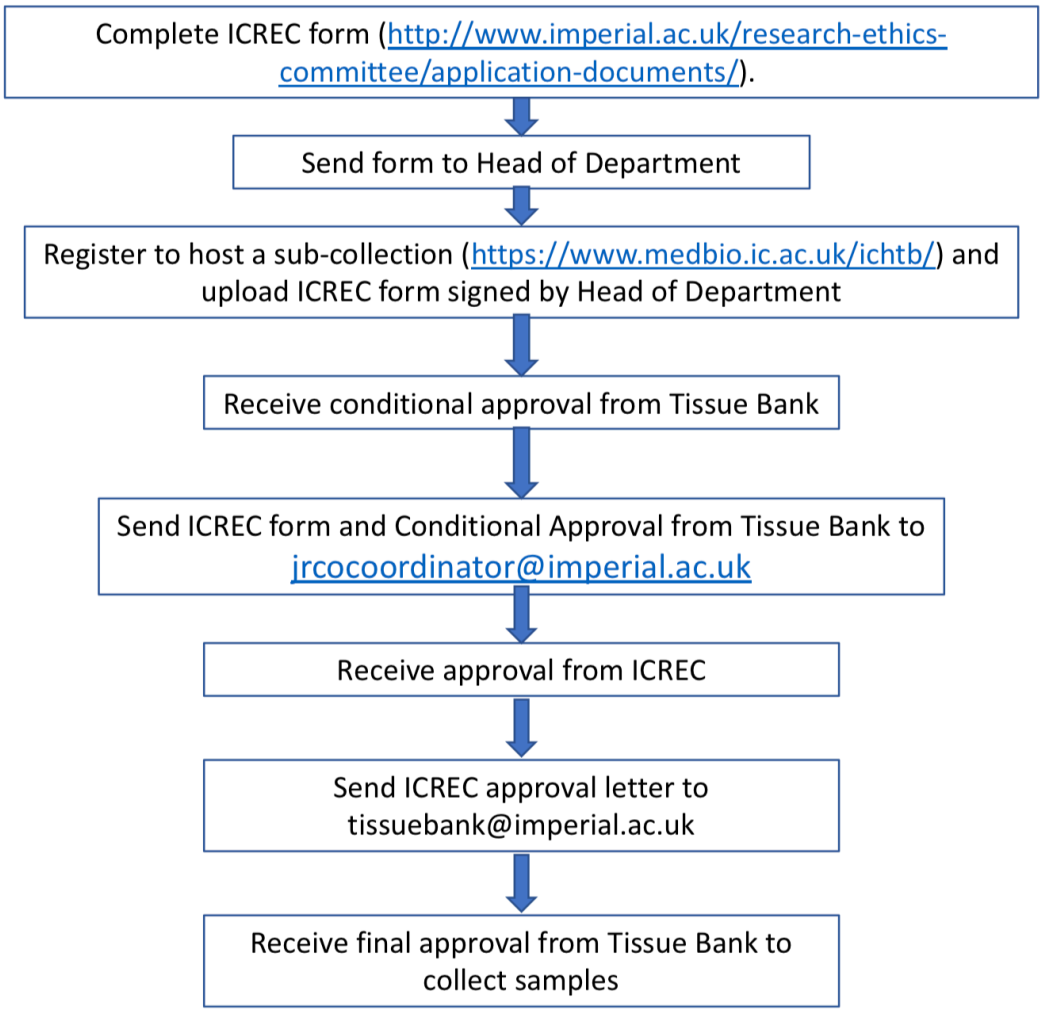
## B.2 Donors who are healthy volunteers – students or staff employed by Imperial College London or Imperial College NHS Trust

Researchers often need samples from a control population. In some cases these samples can be obtained from patients with a different type of disease from the one the researcher is studying, but sometimes a

fluid sample (usually blood) or non-invasive sample (e.g., sweat, saliva, breath, stool or urine) from a healthy person is required. Where the individual is not currently a patient treated by the NHS Trust, consent for acquisition of the sample must be recorded in an appropriate manner. Unlike the situation with patients enrolled in the ICHTB, no information on individual research results will be provided to healthy volunteers and their medical records will not be accessed. Where acquisition of a blood sample is required, venepuncture is carried out by a trained phlebotomist.

Where the target volunteer population and/or PI are staff or students of Imperial College London or of its NHS Trust, approval for the project must be sought via Imperial College Research Ethics Committee ICREC). This approval is around management of the project and to protect the College from allegations of coercion etc. Where appropriate, ICREC may seek approval of the Head of Department of the PI and regard this as equivalent to "Chairman's action" for REC. A flowchart for this procedure is provided below in Figure 6.

Figure 6: Flowchart for sub-collections using the Healthy Volunteer consent materials.




## B.2.1 Recording consent for obtaining fluid samples from a healthy volunteer

Details of the consent procedure and the relevant forms are given in Annex 6. Researchers will be provided with the consent form, the patient information sheet and barcode labels for their samples by the Tissue Bank Secretariat. Copies of the signed consent forms are kept in locked cabinets by the PIs of the studies and samples are labeled with a unique alphanumeric ID related to the subcollection registration number.

### B.2.2 Recording and tracking of samples taken for research from healthy volunteers

Researchers wishing to collect fluid samples for research purposes from healthy volunteers must firstly register their sub-collection on Tissue Bank Database. The form for registration is attached as Annex 1. All samples are given a unique ID that link the sample to the PI and to the PI's department e.g. ONC-GT-01-0001B1 would represent the first blood sample from the first patient in the first registered subcollection for PI GT who is based in the Oncology Department.

## B.3 Specific Research Tissue Banks that use their own consent forms and patient information leaflets

This section relates to only those studies that are still actively consenting patients and accruing samples. Our previous REC approval included the Queen Charlotte's Milk Bank, which is now no longer consenting patients. Samples from this bank are now held under the HTA Licence as an "imported" sub-collection – see section A.2.3 above.

### B.3.1 The Recurrent Miscarriage Tissue Bank

The recurrent miscarriage unit, based at St Mary's Hospital and is now recognised internationally, receiving some 800 new referrals per year and continuing to provide antenatal care for many thousands more couples during their subsequent high risk pregnancies. The tissue bank collects blood samples from the parents, and a sample from the baby's cord, or from the products of miscarriage, depending on the pregnancy outcome. DNA is extracted from the samples for research into the genetics of recurrent miscarriage. Patients are given a leaflet on referral to the clinic and are asked to sign a generic consent form for future research on recurrent miscarriage. The consent materials for the Recurrent Miscarriage Tissue Bank can be found in Annex 7. All samples are pseudonymised and stored as a sub-collection under the Imperial HTA Research Licence (see section A2 above). Applications to use material from the Tissue Bank are made through the HRA approved procedure outlined in section D below.

### B.3.2 Trophoblastic and Germ Cell Tumour Research Bank

Gestational trophoblastic tumours and ovarian germ cell tumours are rare tumours that affect young women of reproductive age. In the UK management of women with trophoblastic disease has been centralised with Charing Cross Hospital being the largest of two centres in the UK that treat women with trophoblastic tumours. This has enabled the unit to gain an international reputation for research and good patient outcomes in this field. Management of ovarian germ cell tumours is now also being centralised with Charing Cross Hospital the major centre for treatment of this condition. The objective of the Trophoblastic and Germ Cell Tumour Research Bank is to collect tissue from molar pregnancies, trophoblastic tumours and germ cell tumours together with blood and saliva samples from patients with these conditions and if appropriate blood and saliva samples from their relatives. The resource will enable us, and others, to apply modern technologies to investigate the biology of these diseases with the aim of improving diagnosis, developing new and more effective treatments and further improving patient outcomes.

Patients providing samples will be given a patient information sheet and asked to sign a generic consent form to provide samples for future research and allow us to contact relatives. Relatives who participate will be provided with a participant information sheet and asked to sign a generic consent form to provide samples for future research. The consent materials for donors to the Trophoblastic and Germ Cell Tumour

Research Bank can be found in Annex 8). All samples are pseudonymised and stored as a sub-collection under the Imperial HTA research licence. Applications to use material will be made through the Imperial College Healthcare Tissue & Biobank (see section D below).

## B.3.3 St Marks Hospital NHS Trust Colorectal Tissue Bank

St Marks Hospital is located in Harrow and is the only hospital in the UK to specialize in colorectal disease. Although co-located geographically with Northwick Park NHS Trust, it has strong links with Imperial College London, with many clinicians holding substantive or honorary Imperial contracts. The St Marks campus is listed as a spoke for the Imperial College HTA Research Licence, and historically had been included in the ICHTB Tissue Bank REC approval, but collection of tissue had been in abeyance for a while. It is now wished to restart collection and to integrate as far as possible with the Imperial systems for Tissue Banking. Patients will be offered the chance to consent to donate either samples leftover from diagnosis or extra samples of blood and biopsy material, as is the case with Imperial College Healthcare NHS Trust patients. Samples will be held at St Marks in a specific sub-collection and covered under the Imperial HTA Research Licence. The consent materials use mirror those used at Imperial only varying with respect to the different Trust specific details that are required. The patient information leaflet and consent forms are provided in Annex 12. Applications to use material will be made through Imperial College Healthcare Tissue & Biobank (see section D below for details).

## B.3.4 Chelsea and Westminster Hospital NHS Foundation Trust Tissue Bank (CWTB)

Chelsea and Westminster Healthcare NHS Foundation Trust operates two hospitals, the Chelsea and Westminster Hospital in Fulham and the West Middlesex University Hospital in Isleworth. The Chelsea and Westminster Hospital has close ties with Imperial College London, and many of the hospital's employees hold research contracts with Imperial College London. The HTA Research Licence has been extended to include the Chelsea campus, to enable collection of human samples from patients treated by C&WT to be used in research by Imperial College academics based at the Chelsea site.

Patients will be offered the chance to consent to donate either samples leftover from diagnosis or extra samples of blood and biopsy material, as is the case with Imperial College Healthcare NHS Trust patients. Samples will be held on the Chelsea campus in specific sub-collections and covered under the Imperial HTA Research Licence. The consent materials use mirror those used at Imperial only varying with respect to the different Trust specific details that are required. The patient information leaflet and consent forms are provided in Annex 13, together with an SOP for consent. Applications to use material will be made through Imperial College Healthcare Tissue & Biobank (see section D below for details).

## B.4 Specific consent for xenograft studies

The HTA has produced guidance that specific consent needs to be sought when tissues from a patient are to be used in xenograft models. If material is being collected with this intent, patients will be asked to sign both the appropriate consent form for ICHTB (see section B1) and an additional consent form. Patients will also be provided with an extra patient information sheet that provides explicit information on what a xenograft is, and its use in research. Consent materials for xenograft studies can be found in Annex 9.

## B.5 Material obtained Post mortem

### B.5.1 Material obtained from standard post mortems

Imperial NHS Trust already has established procedures for consenting family members for post mortems to be carried out for medico-legal reasons. The Trust has embedded consent for research studies into this procedure. The relevant documents are provided in Annex 10.

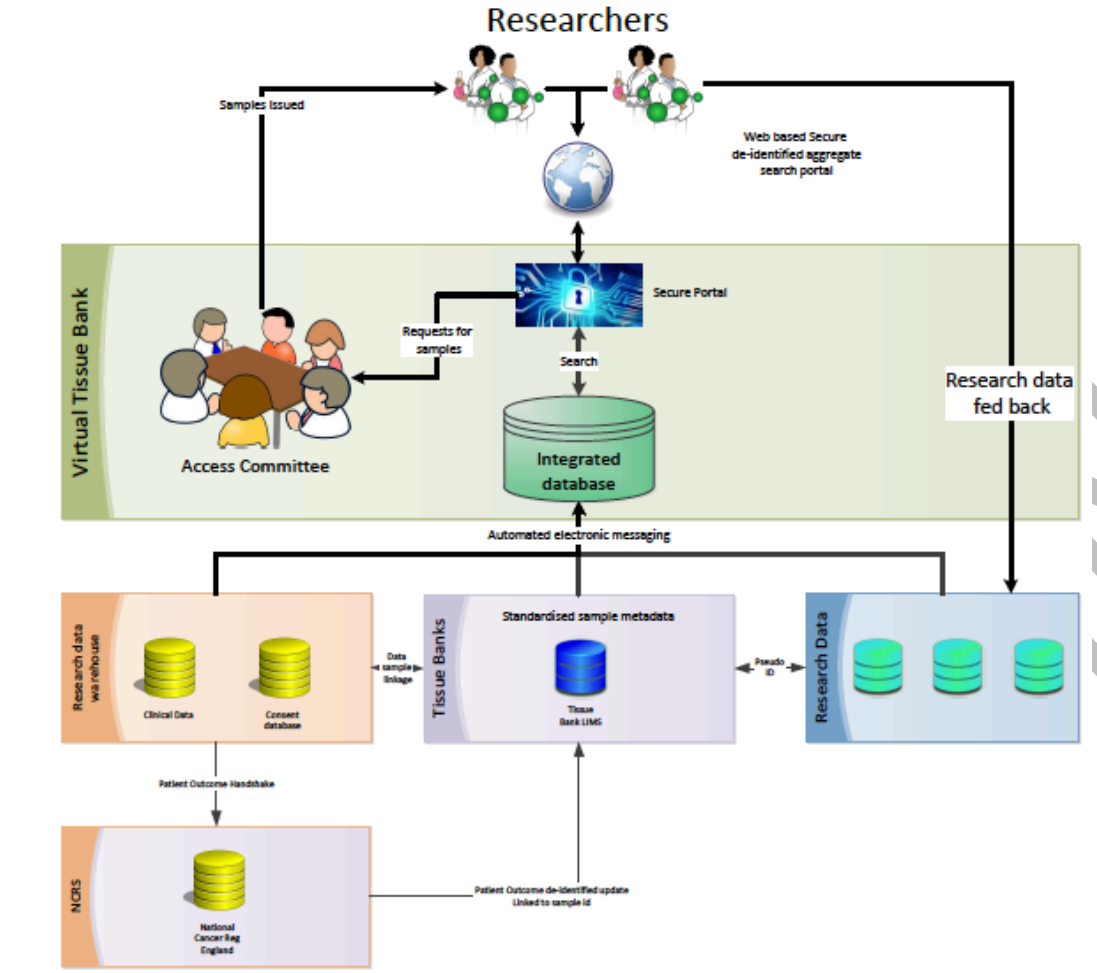
### B.5.2 Material obtained following donation of a body for anatomical examination

Imperial College obtains bodies donated through the London Anatomy Office for anatomical examination for teaching purposes. Donors consent ante mortem and consent is taken for both teaching and research (London Anatomy Office consent forms are included in Annex 10). Donation for research through this mechanism is particularly valuable for projects in bioengineering as access can be gained to whole bones or joints. A researcher using samples from such donors must register a subcollection (see Section A) so that samples can be tracked from the Anatomy Department through to release for individual research projects. All samples are de-identified using the same coding mechanism as for samples taken from living patients or volunteers.

# Section C – Data linkage

## C.1 Sample metadata

To ensure donor confidentiality, biological samples and their clinical information are linked by a unique ID. This ID is issued by the Tissue Bank and is linked to the consent ID recorded on the Trust's consent engine in the case of NHS patients consented for ICHTB (see Figure 4). Where the donor is a healthy volunteer, the ID is allocated by the Tissue Bank database, on registration of a sub-collection. The current database system is shown in Figure 7. Tissue bank staff holding honorary clinical contracts are provided with a username and password by the NHS Trust to log into Trust IT systems, and are able to access metadata on the sample e.g. the pathological diagnosis for the sample, SNOMED code etc. The Tissue Bank database is similarly protected by usernames and passwords and is inside Imperial College's Firewalls. The Tissue Bank database provides not only a method for holding pseudonymised information, but also provide a tracking system for samples. Individual samples can be tracked through processing to different analytes (e.g. DNA, RNA, serum, plasma etc.) through to release to researchers. These data are maintained by tissue bank staff for the subcollection that comprises material left over from operation. Principal Investigators who hold registered sub-collections sign an agreement with the Tissue Bank that they will update accrual of samples into their sub-collection and release of samples to researchers following appropriate approval (see section D). All collections are subject to rolling audit to ensure that the data held on the database is accurate.




The Tissue Bank database is maintained on Imperial College servers at South Kensington with regular back-ups being made and held off site. Each member of Imperial College has a unique numerical ID linked to a user name and password held within the College's LDAP system. The Tissue Bank utilizes this system to provide access to the Tissue Bank database for subcollection users, ensuring that access can be tracked by the College's ICT system. Within the tissue bank database, users are provided with different levels of access depending on their roles. For example subcollection PIs and their nominees can access their own subcollections, researchers can access their own research projects. Only Tissue Bank senior staff have access to the entire database as superusers. The Tissue Bank infrastructure was designed and is managed and developed by Chris Tomlinson.

## C.2 Linkage of consented patients to healthcare data stored in ICHT

When patients are consented for ICHTB, their data held in the hospital medical record can be linked to the patient. A flag will be placed in these datasets to indicate that the patient has consented to ICHTB. The datasets are pseudonymised in the Trust data warehouse before being passed to anyone outside the care team of the patient. Data will only be transferred following appropriate approvals from the Trust Information Governance Team or via an HRA approved mechanism (project specific HRA approval or via the mechanism outlined in Section D).

# Section D – Access to samples for research

We are seeking continuation of approval not only to access material for research that has been taken with consent as outlined above in section C, but also material that has been taken with diagnostic intent and remains within the diagnostic archive stored at our 3 hospital campuses, and subsequently in NHS Trust approved storage off site via Cellnass. Archived material is a potential goldmine for researchers as in some cases it can be linked to a detailed longitudinal dataset that contains information on ultimate patient outcome. However, prior to the advent of the HTA, prospective consent from patients was not sought, and although regarded as good practice by the HTA, the HTA has accepted that material from the diagnostic archive can be accessed without consent providing the material is pseudonymised and that there is a REC approved mechanism for access.

The HTA do insist that consent is a pre-requisite for access to samples obtained post mortem. Our procedure for consent to material obtained post mortem is outlined in Section B5 and Annex 10.

## D.1 Diagnostic Pathology Archive

Imperial College Healthcare NHS Trust has an extensive archive of samples of fluid, and formalin fixed, paraffin embedded (FFPE) material that was taken for diagnostic purposes. Once diagnosis is complete, this material is archived. FFPE material and archived fluids such as serum are very valuable resources for research, as they can be linked to extensive information on how the patient has been treated, and how the patient has responded to treatment. Data can be collated either by tissue bank staff or the specialized clinical team, who are bound by their clinical contracts to respect patient confidentiality, and associated via an pseudonymised link to the pathological biological samples on the Tissue Bank database. FFPE blocks themselves are rarely issued to researchers. Sections from them, with appropriate approval by a pathologist to ensure sufficient residual material remains for unforeseen diagnostic purposes, are cut by tissue bank technicians and issued to researchers using an identification code provided by the tissue bank. The pathology number only is recorded and tracked on the Tissue Bank database. This ensures that patient confidentiality is protected – access to the patient identifiers (hospital number, NHS number, name, address etc) remain on the NHS Trust IT system, but can be linked to the patient via the Pathology number should this be necessary by staff with approved access to the Trust IT system. Data from research studies would not be fed back to patients who had not been approached for consent to use their samples.

## D.2 Procedure for accessing materials for research

The procedure for seeking access to tissue for research, whether the material is taken specifically for research and comes through the consent procedures as outlined in section B, or whether the samples have been taken originally with diagnostic intent (see D1 above) is outlined in Annex 11. Applications for access are made through an on-line system linked to the Tissue Bank database. The SOP for this procedure is detailed in TB-SOP-005 SI. The rules for the use of material from the tissue bank are given in a Material and Data Transfer Agreement TB-DOC-App1. All applications are reviewed by an Application Review Panel using the procedure outlined in TB-DOC-App2. The terms of reference for, and membership of the Application Review Panel can be found in TB-DOC-App4.

Each research project is assigned a unique reference number. Projects that have separate specific REC approval are assigned an N number and those that are approved via the Application Review Panel with “deemed” ethics approval are assigned an R number. The projects are provided with an identifier for the

year and a sequential number e.g. R17001 would be the first project approved through the deemed ethics route in 2017. Each sample with its unique ID is assigned to each individual project. All samples are barcoded. A list of the samples provided to each project is supplied with the samples and the researchers are asked to confirm receipt. All this information is stored on the Tissue Bank database.

## Section E – List of Annexes

### Annex 1: Roles and Responsibilities of PIs of subcollections

TB-DOC-SCM017 – Application for registration as a Sub-Collection under the HTA licence
TB-DOC-SCM9 – Subcollection Report Form Annual Report to ICHTB

### Annex 2: Terms of Reference for, and membership of, the Committee

TB-DOC-RP1 – Tissue Management Committee (TMC) Terms of Reference

### Annex 3: Consent for tissue left over from operative procedure

TB-SOP-002CD – SOP for Recording consent for use in research of material leftover from a procedure
TB-DOC-CF1 – ICHTB Generic Surgical Consent form
TB-DOC-PI1 – ICHTB PIS Information for patients, relatives and carers

### Annex 4: Consent for extra samples tissue from operative procedure

TB-SOP-003CD – SOP for recording consent for Extra samples of fluid or biopsy material taken at the same time at which the same type of sample is being taken for diagnosis
TB-DOC-CF2 – ICHTB Consent Form for Extra Samples
TB-DOC-PI1 – ICHTB PIS Information for patients, relatives and carers

### Annex 5: Return of Results

TB-DOC-M14 – Return of Results policy

### Annex 6: Consent for obtaining fluid samples from healthy volunteers

TB-SOP-004CD – SOP for consenting healthy volunteers
TB-DOC-PI3 – PIS for Healthy Volunteers
TB-DOC-CF3 – Consent form for Healthy Volunteers

### Annex 7: Consent materials for the Recurrent Miscarriage Tissue Bank

TB-DOC-PI12 – PIS for the Recurrent Miscarriage Tissue Bank
TB-DOC-CF9 – Consent form for the Recurrent Miscarriage Tissue Bank

### Annex 8: Consent materials for the Trophoblastic and Germ Cell Tumour Research Bank

TB-DOC-CF10 – Patient consent T&GCT Bank
TB-DOC-CF11 – Relative consent T&GCT Bank
TB-DOC-PI8 – Patient Information Sheet T&GCT Bank
TB-DOC-PI9 – Relative Information Sheet T&GCT Bank

### Annex 9: Consent materials for xenograft studies

TB-DOC-005CD – SOP for consenting patients for Xenograft studies
TB-DOC-PIS4 – Patient Information Sheet for Xenografting
TB-DOC-CF4 Xenografting consent form

## Annex 10: Consent Material for Post Mortem

Adult Post Mortem Examination Consent and Retention of Tissues and Organs Policy – GEN-PD-055-IMP
Paediatric/Perinatal Post Mortem Consent Form – GEN-PD-401-IMP
Paediatric/Perinatal Post Mortem Examination Consent and Retention of Tissues and Organs Policy – GEN-PD-058-IMP
Adult Post Mortem Examination Consent Form – GEN-PD-39-IMP

## Annex 11: Accessing Materials

TB-DOC-App1 – Material Transfer Agreement
TB-DOC-App2 – Process for application to access material from ICHTB
TB-DOC-App3 – Guidance and Terms of Reference for Reviewers of Applications to ICHTB
TB-DOC-App4 – Online Review Guide
TB-DOC-App5 – Project Description form

## Annex 12: Consent material for the St Marks tissue bank

TB-DOC-CF12 – Consent form
TB-DOC-PI19 – St Marks tissue bank PIS

## Annex 13: Consent material for the Consent material for the Chelsea and Westminster Hospital NHS Foundation Trust Tissue Bank (CWTB)

TB-DOC-PI11 – Information for patients, relatives and carers
TB-DOC-CF13 – Consent form (one off treatment)
TB-DOC-CF14 – Consent form (ongoing treatment)
TB-DOC-CF15 – Consent form (provision of extra samples for research)

## Annex 14: E-consenting documents

Screenshot of consenting page
Generated PDF consent form example

## Annex 15: HTA licences