Biomarker Pipeline An NIHR Funded Programme Grant for Applied Research **Study Site Operating Procedure**	Title	TRANSLATIONAL MANUAL: RCC SAMPLE HANDLING				
	Trial Name	Evaluation of Biomarkers for Prognosis of Renal Cell Carcinoma				
	Version	**4**	Date	**22.05.2013**		

Details:

Author(s) of Study Site Operating Procedure: Tobias Wind (NIHR bioRTB)
Michael Messenger (NIHR bioRTB)
Carly Rivers (CTRU)

Comments:

The following Site Specific Procedures are for collection, processing, and distribution of samples for the Renal Cell Carcinoma (RCC) NIHR Biomarker Research Tissue Bank (bioRTB). The objective being to validate biomarkers for prognosis and longitudinal monitoring in patients with renal cell carcinoma

Version Control:

Version number:	Edited by	Date edit completed:	Details of editions made:
2	MPM	09/08/11	Section A, para 3, changed “3, 6” to “3-6”; added F08 to Figure 3 and inserted a diamond symbol in Figures 1 and 2.
3	MPM	20/07/12	Changed process for Forms 04 and 05 to send original and keep a copy. Pg10 corrected text to say “centrifuge both the serum and plasma samples together at room temperature for 10 minutes at 2000 x g (approximately 3000rpm)”. Pg 10 removed statement about recording time serum transferred as only 1 box for both serum and plasma on Form 04.
4	MPM	22/05/13	Updated Section A & Figure 2 to clarify that a final sample is collected on relapse. Confirmed sample processing times in section 2.2

Contents

Section A Introduction

This Study Site Operating Procedure (SSOP) is applicable to the Principal Investigator, Research Nurse, and any other member of staff at research sites who have responsibilities within the Evaluation of Biomarkers for Prognosis of Renal Cell Carcinoma study for the collection and processing of samples for the Leeds NIHR Biomarker Research Tissue Bank (bioRTB).

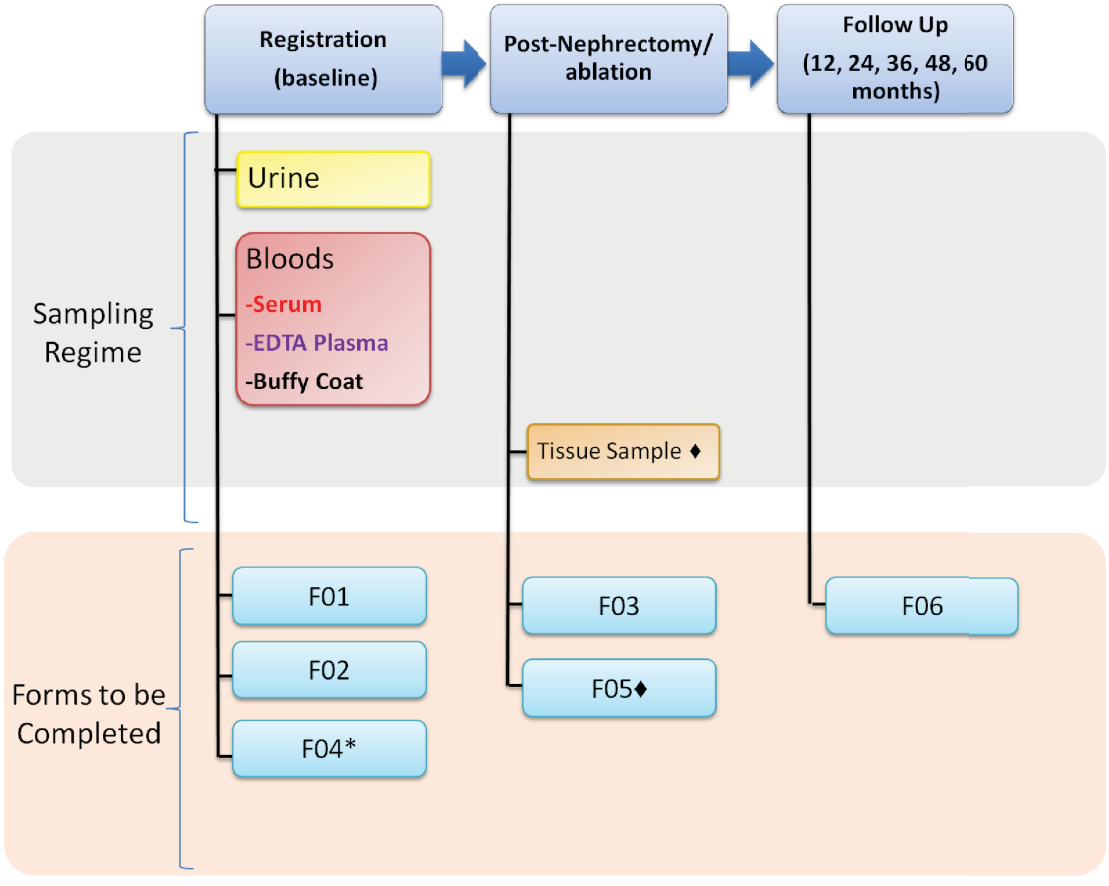
The objective of the study is to validate/qualify prognostic and longitudinal monitoring markers of RCC using prospectively collected high quality clinical samples from multiple centres. Blood, urine and tissue samples will be requested from eligible patients attending participating centres.

Figures 1-3 illustrate the patient/volunteer pathways, their associated sampling regimes and the forms requiring completion at each stage. During the initial 18 months of the study 600 newly diagnosed RCC patients (all stages and histological types) will be recruited onto the cross-sectional arm of the study. RCC patients in the cross-sectional arm are only required to provide a single blood and urine sample at registration and an FFPE tumour tissue block if undergoing nephrectomy (see Figure 1). In the first year, an additional 200 newly diagnosed RCC patients undergoing nephrectomy as part of their treatment regime will be recruited onto the longitudinal arm of the study (see Figure 2). Patients in the longitudinal arm will have baseline blood and urine samples taken at registration and then between 4-60 days post-registration, but prior to nephrectomy. Following nephrectomy an FFPE block of tumour tissue is obtained, followed by further blood and urine samples at 3-6, 12, 18 and 24 months. Sampling will cease earlier if the patient relapses within this time period. However, a final sample must be collected at relapse, prior to initiation of any treatment for the relapse, see Figure 2. All RCC patients in both arms will be followed up annually for a period of up to 5 years. A blood and urine sample is required for healthy control volunteers at registration, with no follow up data required (see Figure 3). In all study arms clinical data is collected at different stages through the use of several case report forms (CRFs). Details of these forms can be found in Table 1.

Table 1: Details of Trial Forms

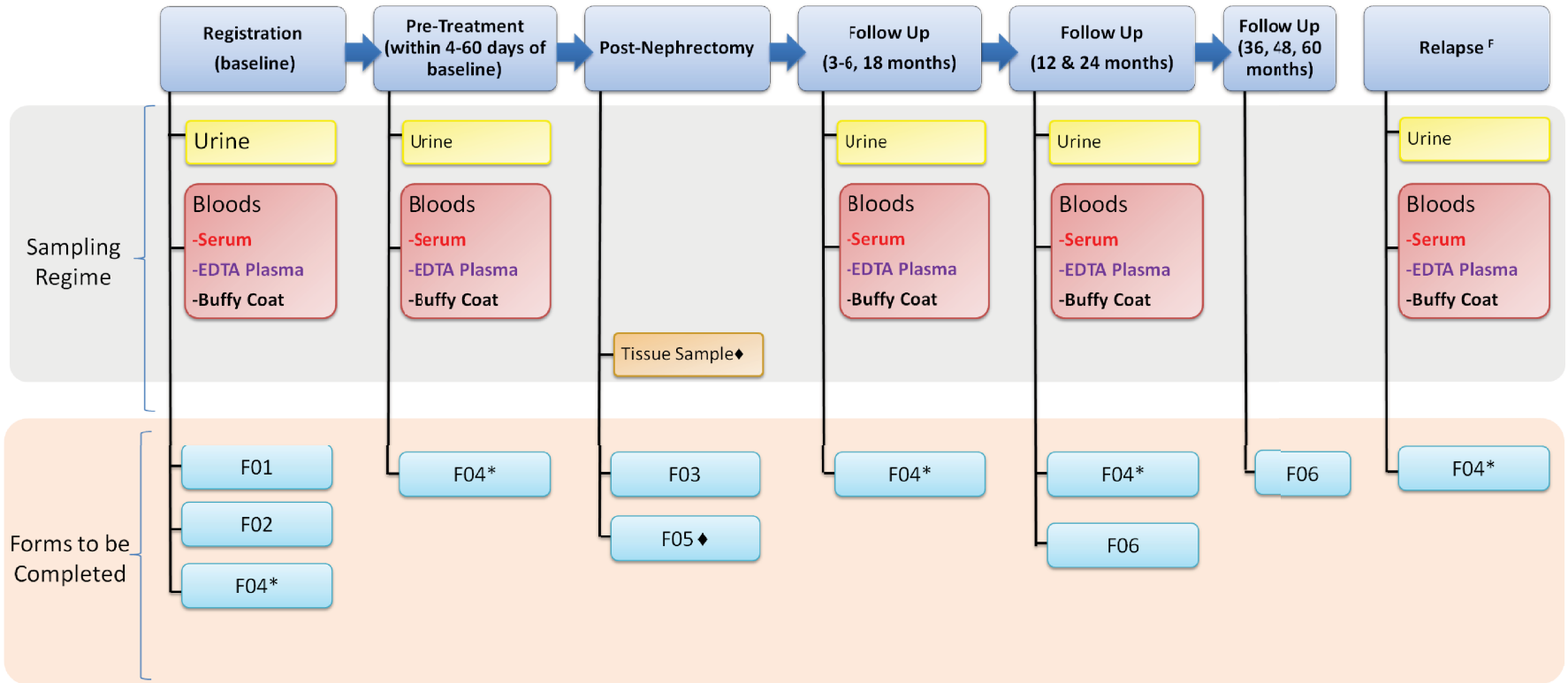
Form	Description
F01	RCC Patient Eligibility & Registration Form
F02	RCC Patient Baseline Assessment Form
F03	RCC Patient Surgery/Ablation/Pathology Details Form
F04	Sample Form
F05	RCC Patient Tissue Sample Form
F06	RCC Patient Follow-Up Form
F07	Healthy Volunteer Eligibility & Registration Form
F08	Healthy Volunteer Baseline Assessment Form

Figure 1: Cross Sectional RCC Patient pathway



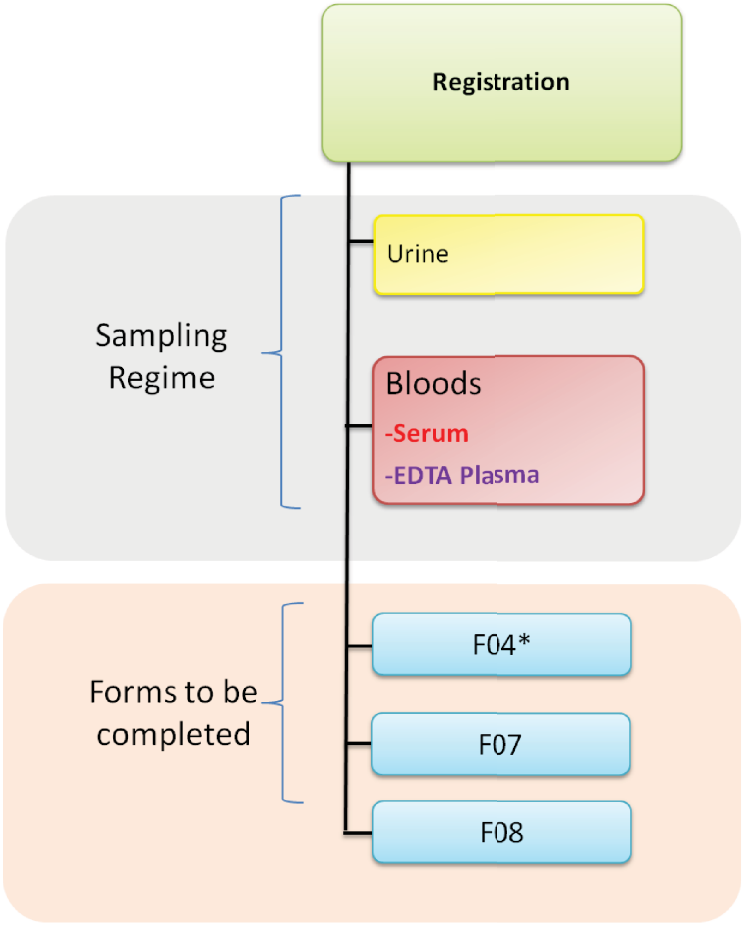
* Included within the sample packs; ♦Only if undergoing nephrectomy

Figure 2: Longitudinal RCC Patient pathway



* Included within the sample packs; ♦Only if undergoing nephrectomy; F Take a final sample at relapse.

Figure 3: Healthy Control Volunteer pathway



* Included within the sample packs

Section B Trial Sample Handling

1. TISSUE SAMPLES

1.1 REQUESTING

Applicable to: Research/Clinical Team

For **all** patients undergoing nephrectomy, an FFPE tumour tissue block should be collected for the research tissue bank (in addition to those normally used for diagnosis).

- Immediately prior to nephrectomy please complete section A of Form 05 "Tissue request form" requesting an additional formalin-fixed paraffin-embedded (FFPE) tumour tissue block and attach to the standard hospital pathology request form sent with the kidney to pathology.

1.2. TISSUE SAMPLE PROCESSING

Applicable to: Histopathology

On receiving the request for an additional FFPE tumour tissue block (Form 05):

1. Ensure the request is logged on the local system according to normal local procedures.
2. Fix and prepare an additional FFPE tumour tissue block according to local standard operating procedures, but do not designate one for research until all blocks/sections have been reviewed as usual by the diagnostic pathologist.
3. Following the usual microscopic diagnostic examination of tumour tissue blocks, designate one for research use in the NIHR biomarker study.
4. Complete section B of Form 05 and pass the form and FFPE tumour tissue block to the local histopathology link person for the study.
5. Within 1 week of designation, the local histopathology link person for the study should complete section C of form 05 and send a copy alongside the designated FFPE block to the NIHR BioRTB, using the pre-addressed safebox packaging provided.

1.3 COLLECTION OF FORM 05

Applicable to: Research/Clinical Team

At locally agreed intervals a member of the research/clinical team should contact the Histopathology link person to arrange collection of the original version of form 05. Following collection, **the original form 05 should be sent to the Leeds CTRU and a copy stored in the investigators site file.**

2. BLOOD & URINE SAMPLES

Applicable to: Research Nurse/Clinician and Sample Processing Team

Two types of sample packs will be provided for processing blood samples: one for the **RCC patient samples** and another for **healthy control volunteer samples**.

The **sample kits** will contain the following:

RCC sample pack:

- Sample Form (Form 04)
- Tube Kit 01 (31 tubes)
- 31 Tube caps
- Pastettes (x4)
- 7 mL Bijou (x2)
- 150 mL Urine Collection Pot
- 50 mL Centrifuge Tube
- 20 mL Barcoded Universal

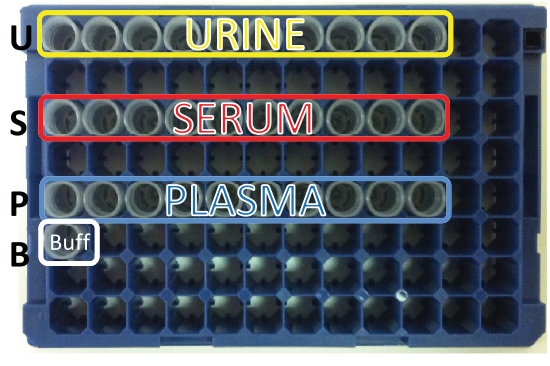
Healthy Control sample pack:

- Sample Form (Form 04)
- Tube Kit 02 (30 tubes)
- 30 tube caps
- Pastettes (x4)
- 7 mL Bijou (x2)
- 150 mL Urine Collection Pot
- 50 mL Centrifuge Tube
- 20 mL Barcoded Universal

Please take extra care to observe the following:

- **Do not mix any of the contents between packs, as all barcodes are unique**
- **Do not move tubes around within the tube kits as their location is pre-defined.**
- **If the tubes accidentally become re-arranged in the rack ensure that you:**
    a. **Put the correct sample type in the correct rack location (see Figure 4)**
    b. **Put the correct coloured lids on the sample tubes (yellow=urine; red=serum blue=plasma; white=buffy coat, see Figure 3)**
    c. **Tell us exactly what happened on the sample form (Kits received without descriptions of errors will fail quality inspection and be discarded).**

***Figure 4: Tube Kit Layout (*Buffy Coat tubes are not included in the Healthy Control Sample Packs)**



2.1 COLLECTION PROCEDURE

1. Ensure the consent form has been completed and copies of the form have been placed in the patient notes (RCC patients only), filing the original in the investigator site file.
2. Select the appropriate **sample pack** and take to the clinic.
3. Record the following information on the **sample form:**
   - Patient/volunteer Initials
   - Patient/volunteer Date of birth
   - Patient/volunteer ID
   - Date sample(s) were taken
   - Manufacturer of blood collection tube(s)
   - Times of venepuncture and urine sample
   - Any comments

Urine sample:

1. Collect urine (mid-stream), directly into the urine collection pot provided.
2. Mark the pot with the patient/volunteer ID, date of birth and initials.
3. Record time of urination on the sample form.
4. Place in bag and then back in pack box (provided).

Blood samples:

Please collect 8-10mL of blood into each tube type using the standard blood collection procedure and apparatus for venepuncture used in your hospital, not via a needle and syringe.

Blood tubes for Serum:

The tubes used for collection of serum samples should be an 8-10 ml plain clot activator tube (silica activator only)

- These tubes are typically red top (serum) when sourced from Greiner and Becton Dickinson; but are white when sourced from Sarstedt.
- Note: Please do not use tubes containing gel or separators for this sample

Blood tubes for plasma:

The tubes used for collection of EDTA Plasma samples should be 4-8 ml Potassium EDTA Plasma tube(s)

- These tubes are typically purple (top) when sourced from Greiner and Becton Dickinson; but are red when sourced from Sarstedt.

PROCEEDURE

1. Collect blood directly into appropriate tube(s). Mix by inverting gently 5 x.
2. Mark the tube(s) with patient/volunteer ID, date of birth and initials.
3. Record time of venepuncture on the sample form (record both times if serum and plasma collected at different times)
4. Place in bag and then back in pack box (provided).

Take all samples for processing immediately to the laboratory within their sample box.

2.2 PROCESSING PROCEDURE

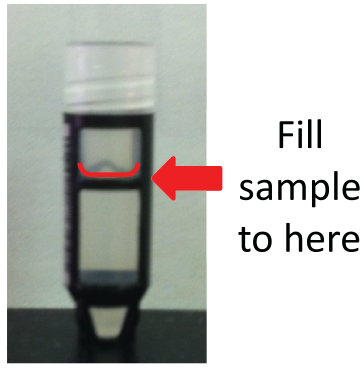
Please refer to Figure 6 for a flow diagram of the sample processing procedure

1. Cross check the IDs on the samples received with the sample form to ensure that the correct blood/urine samples have been received, and that none of the samples are missing.
2. Without removing the clear plastic lid, label the side of the Tube Kit rack with the patient ID, date of birth and initials.
3. Ensure blood samples are left for a **minimum of 45 minutes** post collection (refer to Sample Form: Time of venepuncture) at room temperature. Process blood samples as soon as possible after this time and freeze **within 2 hours** of venepuncture (if this is not possible please make a note in the comments section).
4. Urine samples should be processed at room temperature and frozen **within 2 hours** of collection.

Urine sample:

1. Transfer urine into 50ml centrifuge tube (provided in pack) and label with ID, date of birth and initials.
2. Centrifuge the urine at 2000 x g (approximately 3000rpm in many bench-top centrifuges - needs to be checked as varies with centrifuge type and size) for 10 mins.
3. Using a pastette (supplied) aliquot the urine into the 10 barcoded tubes in **the top row (marked U)** of the Tube Kit (see Figure 4). Fill each tube to just above the central black line (see Figure 5).
4. Place the **yellow** lids on these tubes.
5. Transfer the remaining centrifuged urine into the 20 mL bar-coded Universal (Supplied)
6. Record the time the urine samples were transferred on the Sample Form
7. Replace the lid of tube kit whilst processing blood samples.

Figure 5: Tube fill level (Please avoid overfilling all tubes, as the liquid will expand upon freezing.)



Blood Samples:

After a ***minimum of 45 minutes*** following venepuncture,,centrifuge both the serum and plasma samples together at room temperature for 10 minutes at 2000 x g (approximately 3000rpm).

Serum sample:

1. Use a pastette (supplied) to remove as much of the serum as possible without disturbing the red cell clot. Dispense the serum into the pooling tube (supplied).
2. Aliquot the serum into the 10 bar-coded tubes in the **middle row (marked S)** of the Tube Kit (see Figure 4). Fill each tube to just above the central black line (see Figure 5).
3. Place the **red** lids on these tubes

NOTE: If only a small blood sample was obtained aliquot serum into fewer tubes and discard any unused tubes.

Plasma sample:

1. Use a pastette (supplied) to remove **the upper two thirds** of the plasma to avoid contamination with the buffy coat. Dispense the plasma into the pooling tube (supplied).
2. Aliquot the plasma into the 10 bar-coded tubes in the **lower row (marked P)** of the Tube Kit (see Figure 4). Fill each tube to just above the central black line (see Figure 5).
3. Place the **blue** lids on these tubes
4. Record the time the plasma samples were transferred on the Sample Form

NOTE: If only a small blood sample was obtained aliquot plasma into fewer tubes and discard any unused tubes.

Buffy Coat sample:

(For **Healthy Control** samples skip this step and proceed to "**On Completion of Processing")**

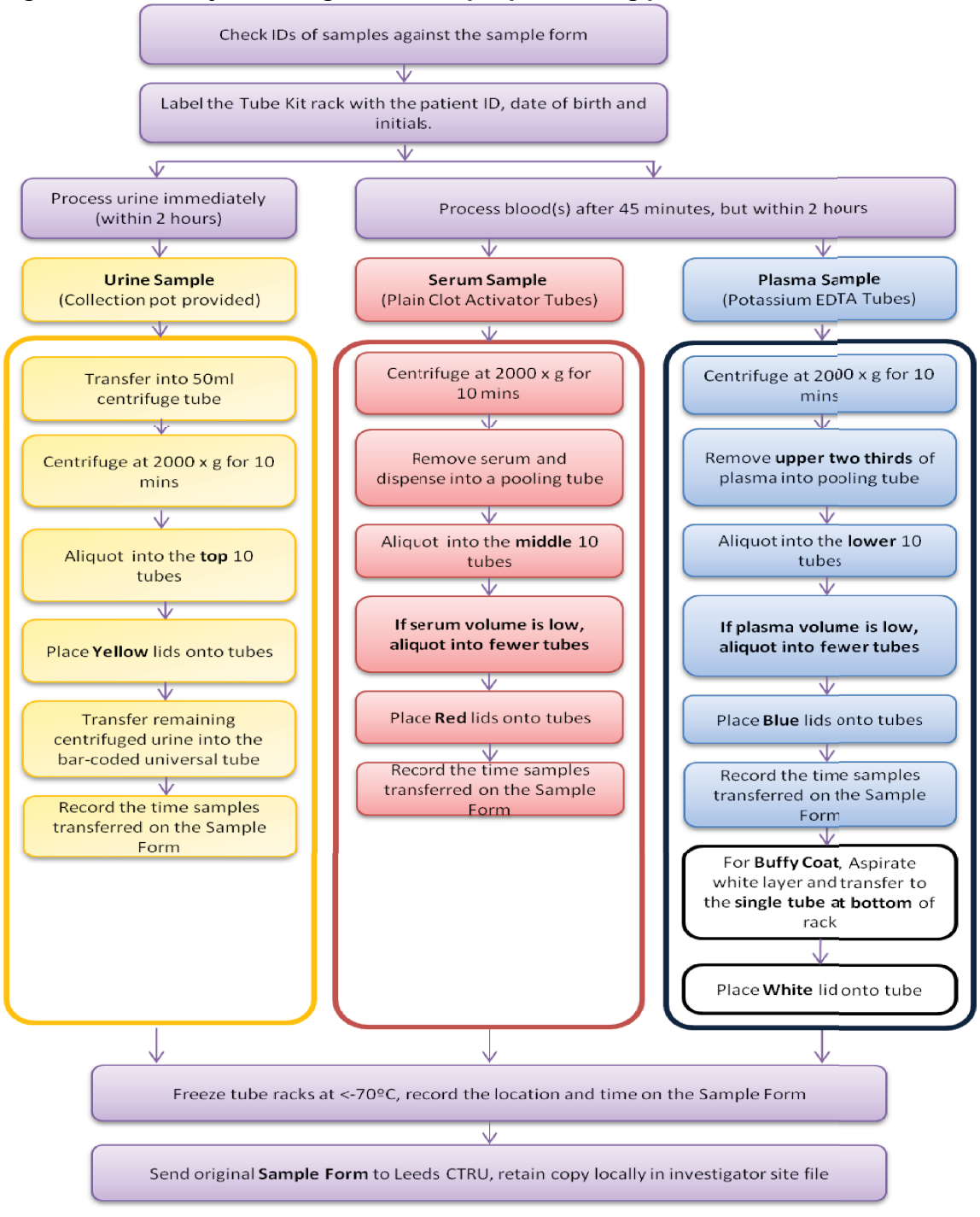
1. Carefully aspirate the white buffy coat layer from the top of the red blood cells using a pastette (supplied) – don't worry if some of the remaining plasma and some of the red blood cells are also collected.
2. Transfer into the solitary tube underneath the plasma samples marked B (see Figure 4).
3. Place the white lid on this tube.

Please refer to Figure 6 for a flow diagram of the sample processing procedure

2.3 ON COMPLETION OF PROCESSING:

1. Immediately store all tubes and Universals in a freezer at a temperature of less than -70ºC.
2. Record the freezer location of the tube racks, and what time they were frozen on Sample Form 04.
3. Send original Sample Form 04 to Leeds CTRU and retain a copy in the site file.

Figure 6: Summary flow diagram of sample processing procedure



3. SHIPMENT PROCEDURE

Frozen samples will be stored at each site until required to be shipped for biobanking. At this time a coordinator from The Leeds NIHR Biomarker Research Tissue Bank will contact you with a request form including a list of all samples to be shipped and details of the courier who will liaise with you over delivery of the packing materials and pick-up date. All shipping materials will be supplied by the courier and must be used as per the instructions in accordance with UN3373 to avoid possible leakage of materials.

Frozen samples:

1. The dry ice and shipment containers will be provided by a courier.

2. Place the locked sample kit boxes and bagged universal tubes into the thermal shipment container. Please note when packing samples they should not be allowed to warm or thaw out and should be kept on dry ice at all times once removed from the freezer and packed as quickly as possible.

3. Fill the thermal shipment container with dry ice to the top, place lid on container.

4. Sign and date the request form, place form in the box and fold over all flaps. The samples are now ready for transportation.

Monitor sample collection and ensure that the samples have been collected as planned – contact the courier if not.

4. QUERIES

If you have any questions, please contact the Study Manager at Leeds CTRU (Tel: [redacted] Fax: [redacted] if it relates to any forms or clinical data; and *Dr Michael Messenger (Tel: [redacted] or [redacted]) if it relates to queries about sample processing or collection*

Biomarker Pipeline An NIHR Funded Programme Grant for Applied Research **Study Site Operating Procedure**	Title	TRANSLATIONAL MANUAL: RENAL TRANSPLANT SAMPLE HANDLING				
	Trial Name	Evaluation of Biomarkers for Post Renal Transplant Complications				
	Version	4.0	Date	31.07.2013		

Details:

Author(s) of Study Site Operating Procedure: Michael Messenger, Tobias Wind, Damien Hindmarch

Comments:

The following Site-Specific Procedures are for collection, processing, and distribution of samples for the Renal Transplant NIHR Biomarker Research Tissue Bank (bioRTB). The objective being to validate biomarkers for diagnosis, prognosis and longitudinal monitoring in patients with renal transplant complications

Version Control:

Version number:	Edited by	Date edit completed:	Details of editions made:
2	MPM	09.03.12	Updated Figure 1
3	MPM	23.04.13	Updated Introduction & Figure 1 to document increased recruitment figures and clarify sample collection points. Table 1 updated to include new forms F01a, F01b & F99. Confirmed sample processing times in section 2.2
4	MPM	31.07.13	Revised Introduction & Figure 1 to account for reduction in sample collection. Samples are to be collected daily for first week of hospital stay, then weekly for one month, then at 2, 3 and 6 months from discharge. Also clarified that sampling and patient participation ends following graft failure, transplant nephrectomy or death

Contents

Section A Introduction

This Study Site Operating Procedure (SSOP) is applicable to the Principal Investigator, Research Nurse, and any other member of staff at research sites who have responsibilities within the Evaluation of Biomarkers for Post Renal Transplant Complications a study for the collection and processing of samples for the Leeds NIHR Biomarker Research Tissue Bank (bioRTB).

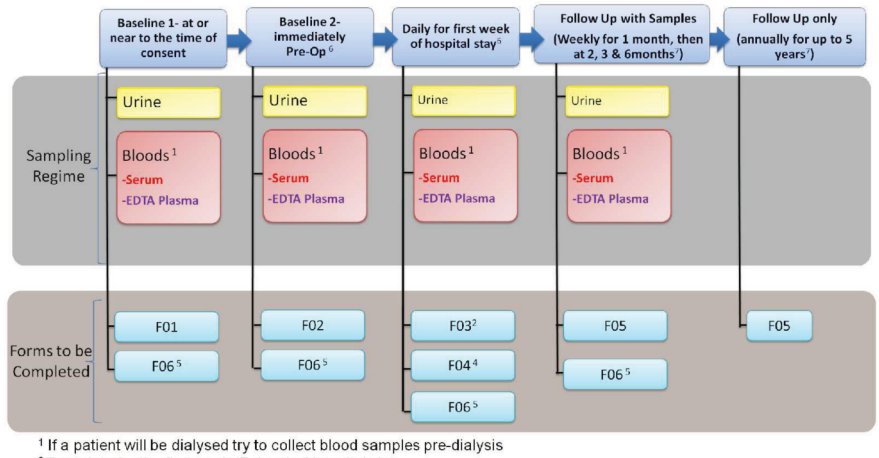
The objective of the study is to validate diagnostic, prognostic and longitudinal monitoring markers of renal transplant complications using prospectively collected high quality clinical samples from multiple centres. Blood and urine samples will be requested from eligible patients attending participating centres.

Figure 1 illustrates the patient pathway, their associated sampling regimes and the forms requiring completion at each stage. Up to 850 patients on the renal transplant waiting list will be recruited onto the study. Patients are required to provide blood and urine samples at baseline (consent and immediately pre-operatively, where possible), daily during the first week of hospital stay, then weekly for 1 month, then at months 2, 3 and 6 (i.e. 6 months from date of discharge). Patients will be followed up annually for a period of up to 5 years. Sample collection and follow up will end if patients suffer graft failure, transplant nephrectomy or death. Clinical data is collected at different stages through the use of several case report forms (CRFs).
Details of these forms can be found in Table 1.

Table 1: Details of Trial Forms

Form	Description
F01a	Eligibility & Registration
F01b	Baseline Assessment
F02	Preoperative Assessment
F03	Post-operative Investigations
F04	Intra/Post-Operative Investigation
F05	Follow-up
F06	Sample Form
F99	Withdrawal

Figure 1: Renal transplant patient pathway



[1] If a patient will be dialysed try to collect blood samples pre-dialysis
[2] Complete for the first week (7 days) of hospital stay
[4] Form completed at the end of hospital stay
[5] Form included within the sample packs
[6] Only collect out of hours (weekend) samples where possible
[7] Follow-up schedule starts once patient is discharged

Section B Trial Sample Handling

1. BLOOD & URINE SAMPLES

Applicable to: Research Nurse/Clinician and Sample Processing Team

Sample packs will be provided for processing blood and urine samples. The sample packs will contain the following:

Renal transplant sample pack:

- Sample Form (Form 06)
- Tube Kit 02 (30 tubes)
- 30 Tube caps
- Pastettes (x4)
- 7 mL Bijou (x2)
- 150 mL Urine Collection Pot
- Medium size bag
- 50 mL Centrifuge Tube
- 20 mL Barcoded Universal

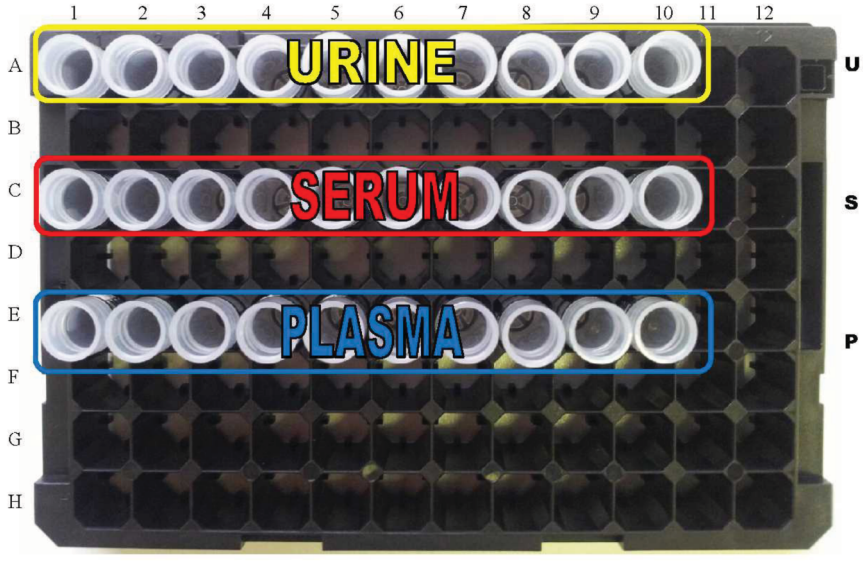
Please take extra care to observe the following:

- **Do not mix any of the contents between packs, as all barcodes are unique**
- **Do not move tubes around within the tube kits as their location is pre-defined.**
- **In the event that tubes are accidentally moved within the rack, ensure that you:**
  a. **Put the correct sample type in the correct rack location (see Figure 2)**
  b. **Put the correct coloured lids on the sample tubes (yellow=urine; red=serum blue=plasma, see Figure 3)**
  c. **Tell us exactly what happened on the sample form (Kits received without descriptions of errors will fail quality inspection and be discarded).**

2.1 COLLECTION PROCEDURE

1. Ensure the consent form has been completed and copies of the form have been given to the patient, placed in the patient notes and the investigator site file.
2. Take a sample kit and record the following information on the **sample form:**
   - Patient/volunteer initials
   - Patient/volunteer date of birth
   - Patient/volunteer ID
   - Date sample(s) were taken
   - Manufacturer of blood collection tube(s)
   - Times of venepuncture and urine sample
   - Any comments

Figure 2: Tube Kit 02 Layout



Urine sample:

1. Collect urine into the urine collection pot provided.
2. Record whether it was collect directly (mid-stream) or via catheter.
3. Mark the pot with the patient ID, date of birth and initials.
4. Record time of sample collection on form F06 and mark whether taken on the same date as the bloods. If not, record urine sampling date.
5. Place in bag and then back in pack box (provided).

Blood samples:

Please collect 8-10mL of blood into each tube type using the standard blood collection procedure and apparatus used in your hospital, not via a needle and syringe

Blood tubes for Serum:

The tubes used for collection of serum samples should be plain clot activator tube (silica activator only)

- These tubes are typically red top (serum) when sourced from Greiner and Becton Dickinson; but are white when sourced from Sarstedt.
- Note: Please do not use tubes containing gel or separators for this sample

Blood tubes for plasma:

The tubes used for collection of EDTA Plasma samples should be Potassium EDTA Plasma tube(s)

- These tubes are typically purple (top) when sourced from Greiner and Becton Dickinson; but are red when sourced from Sarstedt.

PROCEDURE

1. Collect blood directly into appropriate tube(s). Mix by inverting gently 5 x.
2. Record whether blood was collected via venepuncture (preferred) or central line.
3. Mark the tube(s) with patient/volunteer ID, date of birth and initials.
4. Record time of venepuncture on the sample form (record both times if serum and plasma collected at different times)
5. Place in bag and then back in pack box (provided).

Take all samples for processing immediately to the laboratory within their sample box.

2.2 PROCESSING PROCEDURE

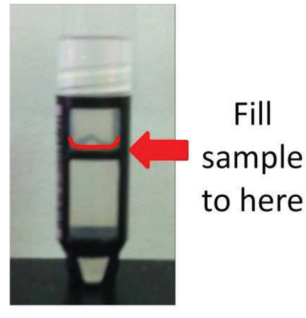
Please refer to Figure 4 for a flow diagram of the sample processing procedure

1. Cross check the IDs on the samples received with the sample form (F06) to ensure that the correct blood/urine samples have been received, and that none of the samples are missing.
2. Label the Tube Kit rack with the patient ID, date of birth and initials.
3. Ensure blood samples are left for a **minimum of 45 minutes** post collection (refer to Sample Form: Time of venepuncture) at room temperature. Process blood samples as soon as possible after this time and freeze **within 2 hours** of venepuncture(if this is not possible please make a note in the comments section).
4. Urine samples should be processed at room temperature and frozen **within 2 hours** of collection**.**

Urine sample:

1. Transfer urine into the centrifuge tube (provided) and label with ID, date of birth and initials.
2. Centrifuge the urine at 2000 x g (approximately 3000rpm in many bench-top centrifuges - needs to be checked as varies with centrifuge type and size) for 10 mins.
3. Using a pastette (provided) aliquot the urine into the 10 barcoded tubes in **the top row (row A, marked U)** of the Tube Kit (see Figure 2). Fill each tube to just above the central black line (see Figure 3).
4. Place the **yellow** lids on these tubes.
5. Transfer the remaining centrifuged urine into the 20 mL bar-coded Universal tube (provided).
6. Record the time the urine samples were transferred on the Sample Form
7. Replace the lid of tube kit whilst processing blood samples.

Figure 3: Tube fill level (Please avoid overfilling tubes, as the liquid will expand upon freezing.)



Blood Samples:

After a ***minimum of 45 minutes*** following venepuncture, centrifuge both the serum and plasma samples together at room temperature for 10 minutes at 2000 x g (approximately 3000rpm).

Serum sample:

1. Use a pastette (provided) to remove as much of the serum as possible without disturbing the red cell clot. Dispense the serum into the pooling tube (provided).
2. Aliquot the serum into the 10 bar-coded tubes in the **middle row (row C, marked S)** of the Tube Kit (see Figure 2). Fill each tube to just above the central black line (see Figure 3).
3. Place the **red** lids on these tubes

NOTE: If only a small blood sample was obtained aliquot serum into fewer tubes and discard any unused tubes, note the number of aliquots on the sample form.

Plasma sample:

1. Use a pastette (provided) to remove **the upper two thirds** of the plasma to avoid contamination with the buffy coat. Dispense the plasma into the pooling tube (provided).
2. Aliquot the plasma into the 10 bar-coded tubes in the **lower row (row E, marked P)** of the Tube Kit (see Figure 2). Fill each tube to just above the central black line (see Figure 3).
3. Place the **blue** lids on these tubes
4. Record the time the blood samples were transferred on the Sample Form

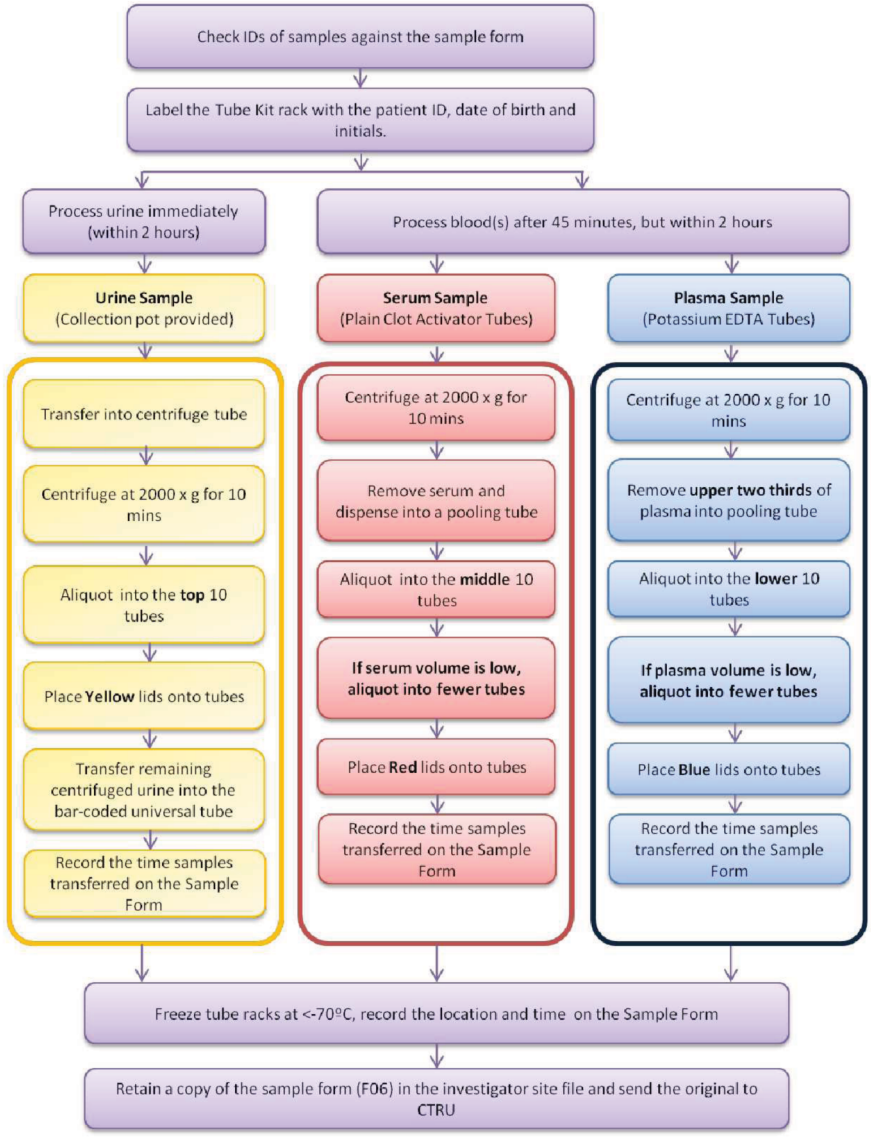
NOTE: If only a small blood sample was obtained aliquot plasma into fewer tubes and discard any unused tubes, note the number of aliquots on the sample form

Please refer to Figure 4 for a flow diagram of the sample processing procedure

2.3 ON COMPLETION OF PROCESSING:

1. Immediately store all tubes and Universals in a freezer at a temperature of less than -70ºC.
2. Record the freezer location of the tube racks, and what time they were frozen on Sample Form 06.
3. Send original Sample Form 06 to Leeds CTRU and retain a copy in the site file.

Figure 4: Summary flow diagram of sample processing procedure



3. SHIPMENT PROCEDURE

Frozen samples will be stored at each site until required to be shipped for biobanking. At this time a coordinator from The Leeds NIHR Biomarker Research Tissue Bank will contact you with a request form including a list of all samples to be shipped and details of the courier who will liaise with you over delivery of the packing materials and pick-up date. All shipping materials will be supplied by the courier and must be used as per the instructions in accordance with UN3373 to avoid possible leakage of materials.

Frozen samples:

1. The dry ice and shipment containers will be provided by a courier.

2. Place the locked sample kit boxes and bagged universal tubes into the thermal shipment container. Please note when packing samples they should not be allowed to warm or thaw out and should be kept on dry ice at all times once removed from the freezer and packed as quickly as possible.

3. Fill the thermal shipment container with dry ice to the top, place lid on container.

4. Sign and date the request form, place form in the box and fold over all flaps. The samples are now ready for transportation.

Monitor sample shipment and ensure that the samples have been collected as planned – contact the courier if not.

4. QUERIES

If you have any questions, please contact the Data Manager at Leeds CTRU (Tel: [redacted] Fax: [redacted] if it relates to any forms or clinical data; and *Dr Michael Messenger (Tel: [redacted]) if it relates to queries about sample processing or collection*

ctru Study Site Operating Procedure	Title	TRIAL SAMPLE HANDLING				
	Trial Name	ELUCIDATE TRIAL				
	Version	3.0	Date	16.11.2010		

Details:

Author(s) of Study Site Operating Procedure: Dr. Michael Messenger (NIHR bioRTB)
Claire Davies (CTRU)
Carly Rivers (CTRU)

Comments:

The following Site Specific Procedures are for collection, processing, and distribution of samples for the ELF test and NIHR Biomarker Research Tissue Bank (bioRTB).

Version Control:

Version number:	Edited by	Date edit completed:	Details of editions made:
1.0	CD	22.09.2010	Section B1 amended to permit use of needle and syringe but to advise that notes should be made on the ELF sample form. Section B3 also amended to request that notes be added to the ELF sample form if the serum sample was not processed in the 2 hour window.
2.0	CD	16.11.2010	Section B5 updated with amended e-mail addresses for CTRU and Biobank lab.

Contents

Section A Applicability

This Study Site Operating Procedure (SSOP) is applicable to the Principal Investigator, Research Nurse, and any other member of staff at the research site who have responsibilities within the ELUCIDATE Trial for the collection, processing and despatch of samples for the ELF test and NIHR Biomarker Research Tissue Bank (bioRTB).

All patients require an ELF test sample to be taken at registration and randomisation. In the ELF arm, follow up samples are to be taken every 6 months. In the control arm a single ELF test will be taken at diagnosis of cirrhosis. A single sample for the NIHR biomarker RTB is **only** taken at **randomisation** in addition to the ELF test sample, refer to Figure 1. Note that patients on heparin are not eligible for the study as the ELF test cannot be performed.

The registration samples should be taken **non-fasted/fed**. Randomisation samples should be taken **fasted**. Follow-up samples should be taken **non-fasted/fed**. For the purposes of this trial, a patient is considered fasted if they have had no food (water only) overnight or for 4 or more hours.

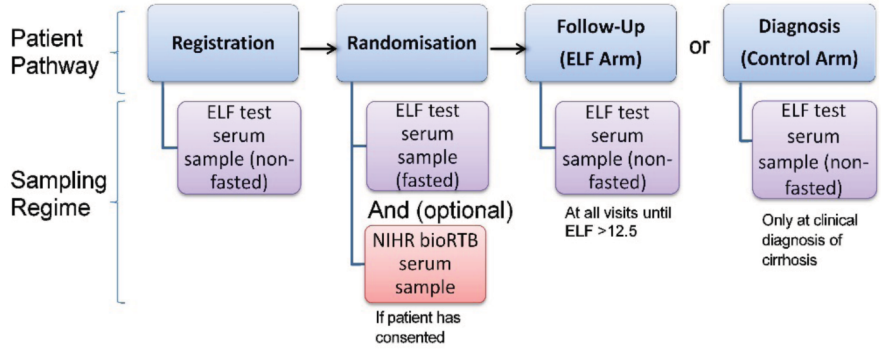


Figure 1: Flow diagram of the patient pathway and associated sampling regimes

Section B Trial Sample Handling

1. SAMPLE KITS AND GENERAL INSTRUCTIONS

Two types of sample kit will be provided for processing blood samples: one for the **ELF Test samples** and another for the **ELF Test and NIHR biomarker RTB samples**.

The **sample kits** will contain the following:

ELF TEST sample kit:

- Sample Form (Form 05)
- ELF Shipping Form
- Pastettes (x2)
- Self-adhesive blood tube label
- 1x purple capped ELF TEST tube
- Pre-paid and addressed Royal Mail Safebox

Randomisation ELF TEST and NIHR Biomarker RTB sample kit:

- Sample Form (Form 09)
- ELF Shipping Form
- 1x purple capped ELF TEST tube
- Pooling Tube
- Pastettes (x3)
- Self-adhesive blood tube labels
- 10 x red capped NIHR bioRTB tubes
- Pre-paid and addressed Royal Mail Safebox

Please do not mix contents between kits as barcodes are unique to each kit/form/sample.

Please collect blood using the standard blood collection procedure and apparatus for venepuncture used in your hospital, preferably not via a needle and syringe. If a needle and syringe must be used then please make a note in the comments section and take care to remove the needle prior to filling the blood tubes. You will need to supply the actual blood collection tubes as below (**do not use tubes containing EDTA or heparin**):

- **The tube used for the ELF TEST serum samples should be a 4-6 ml serum separator tube (SST)**
  - SST tubes are typically red or gold top (serum) depending on the manufacturer and contain a gel.

- **The tubes used for NIHR Biomarker RTB serum samples should be an 8-10 ml plain clot activator tube (silica activator only)**
  - These tubes are typically red top (serum) when sourced from Greiner and Becton Dickinson; but are white when sourced from Sarstedt.
  - Note: Please do not use tubes containing gel or separators for this sample

2. COLLECTION PROCEDURE

1. Ensure the patient consent form has been completed and copies of the form and the patient information leaflet (PIL) have been placed in the patient notes, filing the original in the investigator site file.
2. Identify what stage of the patient pathway (see Figure 1) the patient is at and what procedures they have consented to. Only collect the **NIHR biomarker RTB sample** if at **randomisation** and the patient has consented.
3. Select the appropriate **sample kit** and take to the clinic.
4. Record the following information on the **sample form:**
   - Patient Initials
   - Patient Date of birth
   - Patient ID
   - Date sample(s) were taken
   - Patient fasted/non-fasted*
   - If at Randomisation, whether a NIHR bioRTB sample has been taken.
   - Manufacturer of blood collection tube(s)
   - Any comments

**fasted defined as no food (water only) either overnight or for more than four hours*

For ELF-TEST sample:

1. Collect 4-6 mL blood directly into a **serum separator/gel tube (SST)**. Mix by inverting gently 5 x.
2. Stick the **ELF-TEST** self-adhesive blood tube label (provided in sample kit) to the SST tube and mark-up with patient ID, date of birth and initials.
3. Record time of venepuncture on the **SAMPLE kit bag** and **sample form.**
4. Place back in **kit bag** (provided).

For NIHR Biomarker RTB sample:

1. Collect 8-10 mL blood directly into the **plain clot activator tube**. Mix by inverting gently 5 x.
2. Stick **NIHR bioRTB** self-adhesive blood tube label (provided in kit) to the plain clot activator tube and mark-up with patient ID, date of birth and initials.
3. If different to ELF test, record time of venepuncture on the **SAMPLE kit bag**. (also make a note in the comments section of the sample form).
4. Place back in **kit bag** (provided).

Take all samples for sample processing immediately to the laboratory within a closed sample bag.

3. PROCESSING PROCEDURE

Please refer to Figure 2 for a flow diagram of the sample processing procedure

Cross check the samples received with the sample form to make certain no blood samples are missing. Ensure the sample(s) are left to clot for a ***minimum of 45 minutes*** *post collection (time of venepuncture) at room temperature. As soon as possible after this time and* ***within 2 hours*** (if this is not possible please make a note of the time in the comments section), *centrifuge at room temperature for 10 minutes at 2000 x g (approximately 3000rpm in many bench-top centrifuges - needs to be checked as varies with centrifuge type and size).*

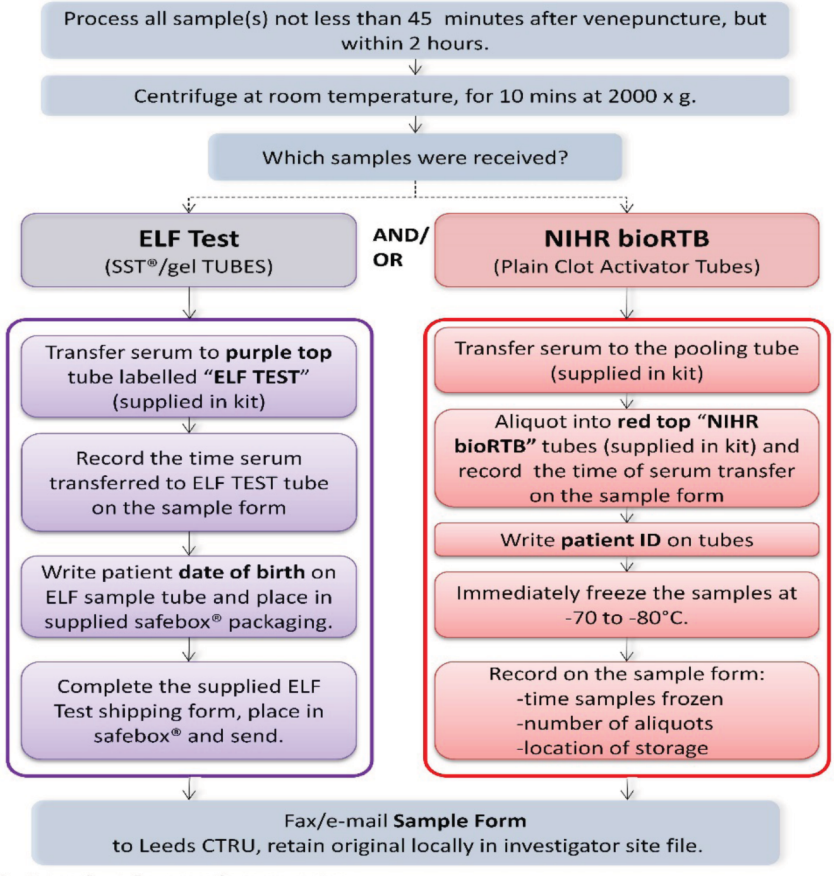


Figure 2: Procedure for sample processing

ELF Test sample: (SST/gel tube)

1. Following centrifugation of the **ELF TEST serum separator/gel tube sample**, use a disposable pastette (supplied) to remove approximately 1ml of the serum, without disturbing the red cells. Transfer serum to purple capped ELF TEST tube (supplied in kit).
2. Record the time the serum was transferred on the sample form.
3. Write the patient **date of birth** on the ELF TEST sample tube in permanent marker. (Please do not write patient ID on the ELF sample)
4. Place the ELF TEST sample in the supplied absorbent packaging, then into the grip-seal bag and finally into the sealable container within the pre-paid safebox® **(Do not close safebox®).**

NOTE: Once the safe box is closed it cannot be re-opened.

5. Complete the supplied **"ELF Test Shipping form"** and retain a copy in the investigator site file. Place original in the safebox®.
6. **Close the safebox®** and send via the normal postal system.
7. Record any issues on the sample form.

NIHR bioRTB sample: (plain clot activator tube)

1. Following centrifugation of the **NIHR bioRTB plain clot activator tube sample,** use a disposable pastette (supplied) to remove as much of the serum as possible without disturbing the red cells. Dispense the serum into the pooling tube (supplied).
2. Using a pastette (supplied), aliquot the serum approximately equally into the 10 **"NIHR bioRTB" red capped tubes** (supplied). If only a small blood sample was obtained and the resulting serum volume is less than 2 mls, aliquot the serum approximately equally into only 5 tubes and discard the other 5 unused tubes.
3. Record the time the serum was transferred on the sample form.
4. Write the **patient ID** on the sample tubes in permanent marker.
5. Within 10 minutes of completion store the **NIHR bioRTB sample tubes (red caps)** in a freezer at a temperature of between -70ºC and -80ºC.
6. Record the number of tubes frozen, location and what time they were frozen on the sample form.
7. Record any issues on the sample form.

N.B. Any deviations from this procedure must be documented on the **sample form**

NIHR bioRTB Shipment Procedure:

Frozen samples will be stored until required to be shipped for banking. At this time a coordinator from The Leeds NIHR Biomarker RTB will contact you to arrange for samples to be collected and shipped. **Contact details can be found below.** The dry ice and shipment containers will be provided by a specialist courier and must be used as per instructions to comply with UN3373 and avoid leakage of materials or personal injury.

On arrival of the courier please do the following:

- Pack the requested samples into the thermal shipment container in the 13x13x5cm storage boxes provided previously by the NIHR bioRTB.
- Fill with dry ice to the top of the thermal shipment container, place lid on unit.
- Sign and date the request form and place in box and fold over all flaps. The samples are now ready for transportation.

4. ON COMPLETION:

Fax/e-mail sample form to Leeds CTRU as described in the final CRF and retain original locally in investigator site file. (Fax: [redacted])

5. ANY QUERIES:

If you have any questions, please contact Claire Davies, Senior Trial Manager at the CTRU (Tel: [redacted])

For queries relating specifically to the NIHR bioRTB samples please contact Dr Michael Messenger (Tel: [redacted])

Renal Cancer Marker Study
PATIENT INFORMATION SHEET

Leeds NIHR Biomarker Research Tissue Bank

We would like to invite you to take part in a research study. Before you decide whether you would like to take part, you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully and discuss it with your family, friends or your GP if you wish. Please take the opportunity to put any questions you may have to a qualified and experienced person. If you decide that you are happy to take part, please sign the attached consent form and have this witnessed. *Keep a copy of this information for future reference.*

What kind of research is being done and why?

Testing human tissue samples and fluids such as urine and blood is necessary to understand how the human body works normally and what changes when things go wrong. We are currently carrying out research into several diseases involving the kidney including renal (kidney) cancer. The main purpose of this research is to develop new clinical tests that can identify changes in the proteins, genes or other substances that we can measure ("biomarkers") in patient samples. These biomarker tests may be used to improve patient care such as helping to diagnose disease earlier or in deciding which drug is having the best effect in a patient.

What am I being asked to donate and what procedures are involved?

Both healthy and unhealthy tissue, cells and fluid samples are important to us as we need to compare them. We are asking you to donate:

- Some kidney tissue if you are having an operation to remove a small bit of your kidney (a biopsy) or all of one of your kidneys (a nephrectomy) as part of your routine treatment. When the surgeons do this, for example as part of your normal care to diagnose your condition, the tissue which is removed goes to the

pathology department where a specialist pathologist will examine it. Often there is spare tissue which they don't need for clinical purposes and we are asking you to donate any unused or spare tissue not needed for your clinical tests. This involves no extra procedures for you at all.

- Blood and urine samples. We would ask your consent to take a small amount of blood (normally less than 20 mls or 5 teaspoons) and/or to provide a urine sample for our research. Often at the hospital you will have a blood sample taken from you ("venepuncture") as a standard part of your clinical care. If you consent to an additional sample for research we would wherever possible take this at the same time through the same needle and therefore avoid any additional needle punctures. If it's not possible and we have to get a sample for research at a different time to your routine venepuncture for clinical blood tests it involves exactly the same process. In all cases this will be carried out by a fully trained member of staff. We will also ask you (if appropriate) if you would be willing to give further samples at other times in the future during your hospital visits.

Donating these samples will not make any difference to the tests that are needed for your clinical care.

Do I have to take part?

No, the decision of whether or not to take part is completely up to you. Deciding to donate or not has no impact on the type or standard of care you receive, now and in the future.

What are the benefits or advantages of taking part?

Research studies usually take many years to complete. You will be contributing to a bank of tissue, cell and fluid samples, which may help to speed up research into

human disease. The results of the research overall may benefit patients with renal cancer in the future. In addition to contributing to generating new knowledge in medical research, it may also decrease the need to rely on testing on animals. However as the research results are about improving care and tests in the future and are not current clinical tests, the results of our experiments on your samples would not be given to you individually.

As an unconditional gift, the benefits of donating tissue, cell and fluid samples are humanitarian rather than personal. You will not receive any financial reward, including from the successful development of any drug or treatment, which might arise from the research and later goes on to make a profit.

What are the risks to me of donating my tissues and fluids?

There are no additional health risks associated with donating samples for research purposes if they are taken as part of a normal diagnostic procedure. If we are taking a blood sample at a different time from your routine tests, the only risks would be minor bruising. If you are a patient and anything in the procedure for obtaining your samples were to go wrong, the normal complaint mechanisms of the NHS are open to you.

What will my samples be used for?

Your samples will be used in various research projects which will involve large-scale analysis of the proteins present in your tissues, cells and fluids to help us understand the biology of your illness and develop new biomarker tests. Samples from some patients may also possibly be involved in studies examining the genetic material (DNA and RNA) and may undergo variety of procedures including whole genome sequencing. This could determine many or all of the features of your DNA but we are interested only in results which are relevant to your illness. None of these results will be passed back to you individually and they will be kept absolutely confidential.

Could any of the results show that I have other illnesses?

It is possible that some of this information may show changes which could be relevant to other illnesses. For example we may find results that show that you are possibly at risk of a genetically determined illness and this may also be relevant to your relatives. As the tests which we carry out are for research purposes only and are not current clinical tests, any results of that kind would need to be considered and investigated properly by a qualified doctor to ensure the information is correct. You have the option of choosing that if such a finding occurs you would like us to keep it absolutely confidential and take no action or we could contact your GP who would then investigate any possibilities with you further using current clinical practice and tests. Also if we are unable to contact you for any reason you can choose whether or not you want us to inform your relatives about these results.

Can I withdraw my consent if I change my mind?

Yes you can if the samples and/or data have not yet been used. Unused data and samples would, after your notice of withdrawal, be disposed of securely and respectfully. If you change your mind and your samples or data have been used, your gift may have already contributed to new knowledge. This cannot be recalled. If you change your mind when you are still in hospital, you can ask a member of your clinical team to inform us on your behalf. If you change your mind later, or you would prefer not to approach us directly, you can write confidentially to our organisation's Research and Development Dept, who will ensure that your wishes are carried out. A standard letter has been given to you for this purpose.

Who will know I am participating in the research?

The only people who will know your identity are hospital staff and a limited number of staff at the Clinical Trials Research Unit where data is stored on secure computers.

All are bound by a professional duty to protect your privacy. An identification number will be assigned to your samples, which ensures that researchers cannot identify you personally from your donation. This will be used in any other databases where details of your donated samples and associated information are stored.

Will any of my personal information be used?

We are asking for your permission for staff to access and use information from your clinical records, including those held electronically. The information we collect will only be that which is relevant to our research and will include general information such as age, gender, any medication you may be on, whether or not you smoke and what kind of diet you eat, as well as information more specifically about your illness such as pathology results, results of routine blood tests and any scan (CT) results and how you respond to different treatments. Access may start at the time you donate your samples and/or be required later e.g. to look at your clinical progress. Before your information is released to researchers, it is anonymised keeping only an identification number. Participants' identities will not be disclosed either to other researchers or when the results of the research are made public.

Who is funding the research?

This study is funded by the National Institute for Health Research (NIHR) but we also receive funding from other sources including Cancer Research UK and the Medical Research Council. Occasionally, we may also receive collaborative grants from companies such as pharmaceutical or diagnostic companies, particularly where we are developing new diagnostic tests in partnership for example. These grants allow us to recover our costs, and any funds we receive in excess of our costs are used to fund further research.

Are there any other third parties involved in the research?

We may collaborate with other researchers in the UK or abroad. They may work in universities, hospitals or the private sector. Your tissue will not, however, be sold for profit.

Who has reviewed the research?

Our research is reviewed by panels of experts associated with the various funding bodies and within academic research internationally. It is also reviewed by relevant ethics committees. This Research Tissue Bank has been approved by Leeds Research Ethics committee on 15th June 2010.

Will I get feedback from the research?

Any findings resulting from the research will be published in scientific or medical journals. Information will be available on the Leeds Teaching Hospitals research website, the NIHR Renal and Liver Biomarkers Programme website (www.biomarkerspipeline.org) and the research group website (www.proteomics.leeds.ac.uk).

Donating to the wider research community?

Other research groups, within Leeds Teaching Hospitals, Leeds University (where the sample bank is based) or elsewhere, are also dependent on donations of tissue, cell and fluid samples to make progress. We would like you to consider whether you would like us to restrict the use of your samples to our research group (and those groups who we work with directly in collaboration), or whether you give us permission to share your samples and associated anonymous data with other research groups. Any project is reviewed by the Research Tissue Bank Management committee, to

make sure that it is scientifically sound and that it fits with the consent that you have given. We will not release any samples unless we are satisfied that our committee has approved the project and the research group has agreed to abide by our conditions. Please tell us what you decide in the consent form.

There are costs involved in storing and sending samples, and we may ask external researchers to contribute to those costs, but we will not make a profit.

Other things to consider

Your tissue may be used for research that involves:

- Export for use in research outside the UK
- Commercial research e.g. developing new tests

Your tissue will not be used for research that involves:

- Research involving therapeutic/reproductive cloning (the latter remaining illegal under the Human Fertilisation and Embryology Authority 2001)
- Research involving human embryos and stem cells
- Research involving animal-human hybrid embryos
- Research into termination of pregnancy or contraception

Who to contact for Further Information:-

If you would like further information you can either

- Ask the person who has provided this booklet to you
- Contact the Principal Investigator,

Professor Peter Selby

Email: [redacted]

Thank you for reading this patient information sheet.

Renal Transplant Marker Study
PATIENT INFORMATION SHEET

Leeds NIHR Biomarker Research Tissue Bank

We would like to invite you to take part in a research study. Before you decide whether you would like to take part, you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully and discuss it with your family, friends or your GP if you wish. Please take the opportunity to put any questions you may have to a qualified and experienced person. If you decide that you are happy to take part, please sign the attached consent form and have this witnessed. *Keep a copy of this information for future reference.*

What kind of research is being done and why?

Testing human fluids such as urine and blood is necessary to understand how the human body works normally and what changes when things go wrong. We are currently carrying out research into several diseases involving the kidney including those involving kidney transplantation. The main purpose of this research is to develop new clinical tests that can identify measurable changes in proteins ("biomarkers") in patient samples. These biomarker tests may be used to improve patient care such as diagnosing disease earlier or in deciding which drug is having the best effect in a patient.

What am I being asked to donate and what procedures are involved?

We are asking you to donate:

Blood and urine samples. We would ask your consent to take a small amount of blood (normally less than 20 mls or 5 teaspoons) and/or to provide a urine sample for our research. Often at the hospital you will have a blood sample taken from you ("venepuncture") as a standard part of your clinical care. If you consent to an additional sample for research we would wherever possible take this at the same time

through the same needle and therefore avoid any additional needle punctures. If it's not possible and we have to get a sample for research at a different time to your routine venepuncture for clinical blood tests it involves exactly the same process. In all cases this will be carried out by a fully trained member of staff. We will also ask you (if appropriate) if you would be willing to give further samples at other times whilst in hospital or in later hospital visits.

Donating these samples will not make any difference to the tests that are needed for your clinical care.

Do I have to take part?

No, the decision of whether or not to take part is completely up to you. Deciding to donate or not has no impact on the type or standard of care you receive, both now and in the future.

What are the benefits or advantages of taking part?

Research studies usually take many years to complete. You will be contributing to a bank of clinical samples which may help to speed up research into human disease. The results of the research overall may benefit patients with renal transplant rejection and delayed graft function in the future. In addition to contributing to generating new knowledge in medical research, it may also decrease the need to rely on testing on animals. However as the research results are about improving care and tests in the future and are not current clinical tests, the results of our experiments on your samples would not be given to you individually.

As an unconditional gift, the benefits of donating samples are humanitarian rather than personal. You will not receive any financial reward, including from the successful

development of any drug or treatment, which might arise from the research and later goes on to make a profit.

What are the risks to me of donating my fluids?

There are no additional health risks associated with donating fluid samples for research purposes if they are taken as part of a normal diagnostic procedure. If we are taking a blood sample at a different time from your routine tests, the only risks would be minor bruising. If you are a patient and anything in the procedure for obtaining your samples were to go wrong, the normal complaint mechanisms of the NHS are open to you.

What will my samples be used for?

Your samples will be used in various research projects which will involve large-scale analysis of the proteins present in your fluids to help us understand the biology of your illness and develop new biomarker tests. None of these results will be passed back to you individually and they will be kept absolutely confidential.

Could any of the results show that I have other illnesses?

As the tests we carry out are for research purposes only we wouldn't use the results for clinical purposes as there is not enough information available to allow us to do this.

Can I withdraw my consent if I change my mind?

Yes you can if the samples and/or data have not yet been used. Unused data and body fluids would, after your notice of withdrawal, be disposed of securely and respectfully. If you change your mind and your samples or data have been used, your

gift may have already contributed to new knowledge. This cannot be recalled. If you change your mind when you are still in hospital, you can ask a member of your clinical team to inform us on your behalf. If you change your mind later, or you would prefer not to approach us directly, you can write confidentially to our organisation's Research and Development Dept who will ensure that your wishes are carried out. A standard letter has been given to you for this purpose.

Who will know I am participating in the research?

The only people who will know your identity are hospital staff and a limited number of staff at the Clinical Trials Research Unit where data is stored on secure computers. All are bound by a professional duty to protect your privacy. An identification number will be assigned to your samples, which ensures that researchers cannot identify you personally from your donation. This will be used in any other databases where details of your donated samples and associated information are stored.

Will any of my personal information be used?

We are asking for your permission for staff to access and use information from your clinical records, including those held electronically. The information we collect will only be that which is relevant to our research and will include general information such as age, gender, what kind of diet you eat or whether you smoke, as well as information more specifically about your illness such as pathology results, results of routine blood tests, any scan results and how you respond to different treatments. Access may start at the time you donate your samples and/or be required later e.g to look at your clinical progress. Before your information is released to researchers, it is anonymised keeping only an identification number. Participants' identities will not be disclosed either to other researchers or when the results of the research are made public.

Who is funding the research?

This study is funded largely by the National Institute for Health Research (NIHR) but we also receive funding from other sources such as Cancer Research UK and the Medical Research Council. Occasionally, we may also receive collaborative grants from companies such as pharmaceutical or diagnostic companies, particularly where we are developing new diagnostic tests in partnership for example. These grants allow us to recover our costs, and any funds we receive in excess of our costs are used to fund further research.

Are there any other third parties involved in the research?

We may collaborate with other researchers in the UK or abroad. They may work in universities, hospitals or the private sector. Your samples will not, however, be sold for profit.

Who has reviewed the research?

Our research is reviewed by panels of experts associated with the various funding bodies and within academic research internationally. It is also reviewed by relevant ethics committees. This Research Tissue Bank has been approved by Leeds Research Ethics committee on 15th June 2010.

Will I get feedback from the research?

Any findings resulting from the research will be published in scientific or medical journals. Information will be available on the Leeds Teaching Hospitals research website, the NIHR Renal and Liver Biomarkers Programme website (www.biomarkerspipeline.org) and on the research group website (www.proteomics.leeds.ac.uk).

Donating to the wider research community?

Other research groups, within Leeds Teaching Hospitals, Leeds University (where the sample bank is based) or elsewhere, are also dependent on donations of body fluids to make progress. We would like you to consider whether you would like us to restrict the use of your samples to our research group (and those groups who we work with directly in collaboration), or whether you give us permission to share your samples and associated anonymous data with other research groups. Any project is reviewed by our Research Tissue Bank management committee, to make sure that it is scientifically sound and that it fits with the consent that you have given. We will not release any samples unless we are satisfied that our committee has approved the project and the research group has agreed to abide by our conditions. Please tell us what you decide in the consent form. There are costs involved in storing and sending samples, and we may ask external researchers to contribute to those costs, but we will not make a profit.

Other things to consider

Your samples may be used for research that involves:

- Export for use in research outside the UK
- Commercial research e.g. developing new tests

Your samples will not be used for research that involves:

- Research involving therapeutic/reproductive cloning (the latter remaining illegal under the Human Fertilisation and Embryology Authority 2001)
- Research involving human embryos and stem cells
- Research involving animal-human hybrid embryos
- Research into termination of pregnancy or contraception

Who to contact for Further Information:-

If you would like further information you can either

- Ask the person who has provided this booklet to you
- Contact the Principal Investigator,

  Professor Peter Selby

  Email: [redacted]

Thank you for reading this patient information sheet.

HEALTHY VOLUNTEERS INFORMATION SHEET

Leeds NIHR Biomarker Research Tissue Bank

We would like to invite you to take part in a research study. Before you decide whether you would like to take part, you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully and discuss it with your family, friends or your GP if you wish. Please take the opportunity to put any questions you may have to a qualified and experienced person. If you decide that you are happy to take part, please sign the attached consent form and have this witnessed. *Keep a copy of this information for future reference.*

What kind of research is being done and why?

Testing human fluids such as urine and blood is necessary to understand how the human body works normally and what changes when things go wrong. We are currently carrying out research into several diseases. These include particularly, but not exclusively, diseases involving the kidney such as renal (kidney) cancer and kidney transplantation. The main purpose of this research is to develop new clinical tests that can identify measurable changes in proteins ("biomarkers") in patient samples. These biomarker tests may be used to improve patient care such as helping to diagnose disease earlier or in deciding which drug is having the best effect in a patient.

What am I being asked to donate and what procedures are involved?

When we find new biomarkers it is important to know what normal levels are by comparing our results in patients with those in normal healthy volunteers or "controls". We are therefore asking you to donate a blood and/or urine sample to allow us to do this.

We would ask your consent to take a small amount of blood (normally less than 20 mls or 5 teaspoons) and/or to provide a urine sample for our research. Often at the hospital or at your GP you will have a blood sample taken from you ("venepuncture") as a standard part of your clinical care. To get a sample for research involves exactly the same process. In all cases this will be carried out by a fully trained member of staff.

Do I have to take part?

No, the decision of whether or not to take part is completely up to you.

What are the benefits or advantages of taking part?

Research studies usually take many years to complete. You will be contributing to a bank of fluid samples, which may help to speed up research into human disease. The results of the research overall may benefit patients with a range of kidney diseases including renal cancer, renal transplantation and acute kidney injury in the future. In addition to contributing to generating new knowledge in medical research, it may also decrease the need to rely on testing on animals.

As an unconditional gift, the benefits of donating blood and urine samples are humanitarian rather than personal. You will not receive any financial reward, including from the successful development of any test or treatment, which might arise from the research and later goes on to make a profit.

What are the risks to me of donating my fluids?

There is a risk of minor bruising when taking blood samples. If anything in the procedure for obtaining your samples were to go wrong, the normal complaint mechanisms of the NHS are open to you.

What will my samples be used for?

Your samples will be used in various research projects which will involve large-scale analysis of the proteins present in your fluids to help us understand the biology of diseases and develop new biomarker tests. None of these results will be passed back to you individually and they will be kept absolutely confidential.

Could any of the results show that I have other illnesses?

As the tests we carry out are for research purposes only we wouldn't use the results for clinical purposes as there is not enough information available to allow us to do this.

Can I withdraw my consent if I change my mind?

Yes you can if the samples and/or data have not yet been used. Unused data and samples would, after your notice of withdrawal, be disposed of securely and respectfully. If you change your mind and your samples or data have been used, your gift may have already contributed to new knowledge. This cannot be recalled. If you change your mind later, or you would prefer not to approach us directly, you can write confidentially to our organisation's Research and Development Dept who will ensure that your wishes are carried out. A standard letter has been given to you for this purpose.

Who will know I am participating in the research?

The only people who will know your identity are hospital staff and a limited number of staff at the Clinical Trials Research Unit where the data is stored on secure computers. All are bound by a professional duty to protect your privacy. An identification number will be assigned to your samples, which ensures that researchers cannot identify you personally from your donation. This will be used in

any other databases where details of your samples are stored. A limited amount of information will be collected from you by the person obtaining your consent. This includes information such as your age, gender, brief medical history and details of lifestyle factors such as smoking and diet.

Who is funding the research?

This study is funded largely by the National Institute for Health Research (NIHR) but we also receive funding from other sources such as Cancer Research UK and the Medical Research Council. Occasionally, we may also receive collaborative grants from companies such as pharmaceutical or diagnostic companies, particularly where we are developing new diagnostic tests in partnership for example. These grants allow us to recover our costs, and any funds we receive in excess of our costs are used to fund further research.

Are there any other third parties involved in the research?

We may collaborate with other researchers in the UK or abroad. They may work in universities, hospitals or the private sector. Your samples will not, however, be sold for profit.

Who has reviewed the research?

Our research is reviewed by panels of experts associated with the various funding bodies and within academic research internationally. It is also reviewed by relevant ethics committees. This Research Tissue Bank has been approved by Leeds Research Ethics committee on (15th June 2010).

Will I get feedback from the research?

Any findings resulting from the research will be published in scientific or medical journals. Information will be available on the Leeds Teaching Hospitals research

website, the NIHR Renal and Liver Biomarkers Programme website (www.biomarkerspipeline.org) and on the research group website (www.proteomics.leeds.ac.uk).

Donating to the wider research community?

Other research groups, within Leeds Teaching Hospitals, Leeds University (where the sample bank is based) or elsewhere, are also dependent on donations of body fluids to make progress. We would like you to consider whether you would like us to restrict the use of your samples to our research group (and those groups who we work with directly in collaboration), or whether you give us permission to share your samples and associated anonymous data with other research groups. Any project is reviewed by our Research Tissue Bank management committee, to make sure that it is scientifically sound and that it fits with the consent that you have given. Please tell us what you decide in the consent form. There are costs involved in storing and sending samples, and we may ask external researchers to contribute to those costs, but we will not make a profit.

Other things to consider

Your samples may be used for research that involves:

- Export for use in research outside the UK
- Commercial research e.g. developing new tests

Your samples will <u>not</u> be used for research that involves

- Research involving therapeutic/reproductive cloning (the latter remaining illegal under the Human Fertilisation and Embryology Authority 2001)
- Research involving human embryos and stem cells
- Research involving animal-human hybrid embryos
- Research into termination of pregnancy or contraception

Who to contact for Further Information:-

If you would like further information you can either

- Ask the person who has provided this booklet to you
- Contact the Principal Investigator,

  Professor Peter Selby

  Email: [redacted]

Thank you for reading this information sheet.

Renal Cancer Marker Study Patient Consent Form

Leeds NIHR Biomarker Research Tissue Bank

Please indicate your understanding of the research study and your consent to take part by initialling (NOT ticking) each of the boxes below.

Please Initial:

I have read and understand the patient information sheet "Leeds NIHR Biomarker RTB RCC Patient Information Sheet Version 1.3 January 2011" and have had the opportunity to ask questions. These have been answered clearly and satisfactorily and I understand the risks and benefits of donating my samples for research. ☐

I give permission for my fluid and cell samples, and tissue samples which are not needed for diagnosis, to be collected and used in scientific research by the Leeds NIHR Biomarker Programme Group and their collaborators (including commercial companies), **including / not including (delete as appropriate)** in large scale genomic studies. ☐

If any of the research findings provide other information which may be relevant to me personally or my relatives such as risk of other illnesses, **I would / would not (delete as appropriate)** like my GP to be contacted to investigate this further. If I can't be contacted **I do / do not (delete as appropriate)** give permission for you to contact my relatives about this ☐

Name of Contact:_____

I do / I do not (delete as appropriate) give permission for my tissue and fluid samples to be shared with other research groups for projects approved by the Leeds NIHR Biomarker RTB Management Committee. ☐

I agree for my details (which will include my name, date of birth, gender, NHS number, and postcode) to be registered with the Medical Research Information Service (MRIS) or traced via the NHS Information Service or relevant patient registries so that information about my health status may be obtained by researchers if necessary. ☐

I give permission for this information about me, provided by me or found in my medical and other health related records to be supplied to and stored by researchers, including electronically, in an anonymous way that protects my identity. I understand that my anonymised samples and data may be shared on a collaborative basis with researchers in other UK centres and, potentially, centres abroad, including outside the European Economic Area (EEA). ☐

I understand that:

- my participation is voluntary and that I am free to decline to give my consent or to withdraw from the study at any time without having to give a reason and that opting out at any stage has no bearing on my legal rights or subsequent medical treatment. ☐
- if I withdraw consent, any samples and data which have already been used in research before that date cannot be withdrawn but unused samples will be disposed of respectfully and my data will no longer be used. ☐

I understand and agree that I will not personally benefit, financially or medically, from my gift of tissue and fluid samples. This includes if my samples are involved in research leading to a new treatment or medical test. ☐

I confirm that I offer my tissue and fluid samples as an unconditional gift and do not wish to place any restriction on the research that will be carried out on them, beyond the limits stated in the information which I have already read. ☐

I agree to a copy of this Consent Form being sent to the Clinical Trials Research Unit (CTRU). ☐

Patient's signature: _____ **Date:**_____

Full name of patient (please print): _____

Patient trial ID number: _____

Signature of person taking consent: _____ **Date:** _____

Full name of person taking consent (please print): _____

Thank you for agreeing to take part in this research.

Renal Transplant Marker Study Patient Consent Form

Leeds NIHR Biomarker Research Tissue Bank

Please indicate your understanding of the research study and your consent to take part by initialling (NOT ticking) each of the boxes below.

Please Initial:

I have read and understand the patient information sheet "Leeds NIHR Biomarker RTB Renal Transplant Patient Information Sheet Version 1.3 January 2011" and have had the opportunity to ask questions. These have been answered clearly and satisfactorily and I understand the risks and benefits of donating my samples for research. ☐

I give permission for my fluid and cell samples, and tissue samples which are not needed for diagnosis, to be collected and used in scientific research by the Leeds NIHR Biomarker Programme Group and their collaborators (including commercial companies). ☐

I do / I do not (delete as appropriate) give permission for my tissue and fluid samples to be shared with other research groups for projects approved by the Leeds NIHR Biomarker RTB Management Committee. ☐

I agree for my details (which will include my name, date of birth, gender, NHS number, and postcode) to be registered with the Medical Research Information Service (MRIS) or traced via the NHS Information Service or relevant patient registries so that information about my health status may be obtained by researchers if necessary. ☐

I give permission for this information about me, provided by me or found in my medical and other health related records to be supplied to and stored by researchers, including electronically, in an anonymous way that protects my identity. I understand that my anonymised samples and data may be shared on a collaborative basis with researchers in other UK centres and, potentially, centres abroad, including outside the European Economic Area (EEA). ☐

I understand that:

- my participation is voluntary and that I am free to decline to give my consent or to withdraw from the study at any time without having to give a reason and that opting out at any stage has no bearing on my legal rights or subsequent medical treatment. ☐
- if I withdraw consent, any samples and data which have already been used in research before that date cannot be withdrawn but unused samples will be disposed of respectfully and my data will no longer be used. ☐

I understand and agree that I will not personally benefit, financially or medically, from my gift of tissue and fluid samples. This includes if my samples are involved in research leading to a new treatment or medical test. ☐

I confirm that I offer my tissue and fluid samples as an unconditional gift and do not wish to place any restriction on the research that will be carried out on them, beyond the limits stated in the information which I have already read. ☐

I agree to a copy of this Consent Form being sent to the Clinical Trials Research Unit (CTRU). ☐

Patient's signature: _____ Date: _____

Full name of patient (please print): _____

Patient trial ID number: _____

Signature of person taking consent: _____ Date: _____

Full name of person taking consent (please print): _____

Thank you for agreeing to take part in this research.

Healthy Volunteer Consent Form

Leeds NIHR Biomarker Research Tissue Bank

Please indicate your understanding of the research study and your consent to take part by initialling (NOT ticking) each of the boxes below.

	Please Initial:
I have read and understand the patient information sheet "Leeds NIHR Biomarker RTB Healthy Volunteer Information Sheet Version 1.3 January 2011" and have had the opportunity to ask questions. These have been answered clearly and satisfactorily and I understand the risks and benefits of donating my samples for research.	☐
I give permission for my fluid and cell samples, and tissue samples which are not needed for diagnosis, to be collected and used in scientific research by the Leeds NIHR Biomarker Programme Group and their collaborators (including commercial companies)	☐
I do / I do not (delete as appropriate) give permission for my tissue and fluid samples to be shared with other research groups for projects approved by the Leeds NIHR Biomarker RTB Management Committee.	☐
I give permission for this information about me, provided by me or found in my medical and other health related records to be supplied to and stored by researchers, including electronically, in an anonymous way that protects my identity. I understand that my anonymised samples and data may be shared on a collaborative basis with researchers in other UK centres and, potentially, centres abroad, including outside the European Economic Area (EEA).	☐
I understand that:	
• my participation is voluntary and that I am free to decline to give my consent or to withdraw from the study at any time without having to give a reason and that opting out at any stage has no bearing on my legal rights or subsequent medical treatment.	☐
• if I withdraw consent, any samples and data which have already been used in research before that date cannot be withdrawn but unused samples will be disposed of respectfully and my data will no longer be used.	☐
I understand and agree that I will not personally benefit, financially or medically, from my gift of tissue and fluid samples. This includes if my samples are involved in research leading to a new treatment or medical test.	☐
I confirm that I offer my tissue and fluid samples as an unconditional gift and do not wish to place any restriction on the research that will be carried out on them, beyond the limits stated in the information which I have already read.	☐
I agree to a copy of this Consent Form being sent to the Clinical Trials Research Unit (CTRU).	☐

Volunteer's signature: _____ Date: _____

Full name of Volunteer (please print): _____

Volunteer's trial ID number: _____

Signature of person taking consent: _____ Date: _____

Full name of person taking consent (please print): _____

Thank you for agreeing to take part in this research.