UNIVERSITY OF LIVERPOOL GCP labs LCTU	**LCTU GCPLab** **Standard Operating Procedure** **SAMPLE COLLECTION, RECEPTION AND TISSUE STORAGE FOR THE PANCREAS BANK**

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Revision History

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1	10/12/2010	30/03/2011	Process updated and amended (see change control for more information)	1283
2	31/05/2011	20/09/2013	Removed section about adding adverse events as there is a general SOP covering this already	2919
3	03/04/2014	13/10/2016	Removed references to shared calendar	5828
4	03/12/2016	20/11/2018	Addition of Paxgene sample collection, typos corrected & reference to Prof Neoptolemos removed	8365

CONTENTS

1. WHO?

This Standard Operating Procedure (SOP) applies to all Clinical Research Fellows delegated to consent and collect pancreas samples from patients undergoing surgery. This SOP applies to the Good Clinical Laboratory Practice (GCP) laboratory technician(s) who have been delegated to store the collected tissue in the GCP Lab Facility.

2. BACKGROUND

The collection of human tissue is a serious matter and is governed by the Human Tissue Act (2004) and EU Directives on research governance. It is the responsibility of each individual to have read and understood the relevant documentation in order to abide by the regulations.

A major activity of the Department of Molecular and Clinical Cancer Medicine (DMCCM) is the collection and storage of human pancreas tissue for translational research. The consenting, collecting and storage of some of the tissues surplus to diagnostic requirement organised by the Liverpool Tissue Bank, University of Liverpool is strongly supported by the DMCCM.

Thus all General Surgical Research Fellows within the DMCCM are required to participate in the Pancreas Rota (Panc Rota) to store samples for ethically approved future research in the Pancreas Biobank. There are no exceptions.

The reason for this is based on straightforward utilitarian principles. By including in the rota all Clinical Research Fellow with knowledge of the abdomen the individual burden is minimized. The collection of pancreas tissues cannot be on an ad hoc basis. The reliable collection processes for benign pancreas and for neoplastic pancreas samples are inter-dependent.

Each Research Fellow is assigned a week on the rota. Samples are collected for the 'Panc Rota' on a daily basis and refers to the process of patient consent, collection and storage of human tissue samples from patients with pancreas disorders and where relevant control subjects.

A senior Clinical Research Fellow in their second or third year of research is delegated to organise the rota taking into account any particular issues from individual Fellows. The senior Fellow carries the delegated authority of the Human Materials Tissue Officer and the Head of Division. There will also be a named Deputy to the Senior Clinical Research Fellow.

Generally, pancreas surgery takes place every weekday as follows:

- **Monday: Mr M Raraty**
- **Tuesday: Mr CM Halloran**
- **Wednesday: Professor P Ghaneh**
- **Thursday: Professor R Sutton / Mr CM Halloran**
- **Friday: Not assigned to an individual consultant**

Any issues relating to tissue collection should be referred directly to the GCP Lab Operations Director (OD) Professor W Greenhalf, or to the Principal Investigator relating to pancreas tissue research, Paula Ghaneh.

The Quality Assurance Manager should be informed of all SOP deviations with respect to the samples.

3. PURPOSE

This SOP has been written to provide uniform procedures for the collection of blood, urine, tissue and juice samples from pancreatic cancer and pancreatitis patients for research use.

4. SCOPE

This SOP applies to all Clinical Research Fellows delegated to the Panc Rota and the GCP laboratory staff who may store the collected tissue in the GCP Facility.

5. PROCEDURE

5.1 REPSONSIBILITY

5.1.1 Responsibilities of the Senior Research Fellow:

It is the responsibility of the Senior Research Fellow to:

- Ensure that the Panc Rota is sent out in advance to all Clinical Research Fellows and the GCP Lab OD. The Rota will also be displayed in Theatres 5 and 7 and updated on a monthly basis.
- Liaise with the LTB, pathologists, GCP technician and Histology department to ensure completion of the SOP and the correct collection and distribution of the samples.

5.1.2 Responsibilities of the Rostered Research Fellow:

It is the responsibility of the Rostered Research Fellow to:

- Ensure that relevant staff are aware on a day-to-day basis how they can be contacted immediately.
- Find out when pancreas surgery is due to take place prior to tissue collection, by 12 noon on Friday the week before. The Research Fellow must also check that no changes have been made. The GCP Lab technicians responsible for the pancreas rota should be informed of planned collections.
- Check with an appropriate member of theatre staff whether the operation is taking place.
- Obtain information regarding elective pancreas surgery from the elective lists or diaries held by the secretaries of individual consultants, as well as more up to date information held by the registrars on the Professional Unit.
- Obtain informed consent from the patient at least one day prior to surgery following the protocol detailed in this SOP.
- Obtain blood and urine samples from the patient as outlined in this SOP.

- Collect relevant patient details and complete the 'Patient data sheet for pancreatic research' and deliver this, along with the consent form and the samples to the GCP Lab Technician.

- Keep the GCP Lab Technician informed about whether the operation is proceeding, when samples are expected and when the samples have been delivered.

- Liaise with the manager of the LTB (Extension 9103 or bleep 680; Liverpool Tissue Bank, 3rd floor William Duncan Building) and the Consultant Pathologist to whom the specimen will be delivered and ensure that contact informations is exchanged. The Research Fellow must ensure the integrity of the sample is maintained and the chain of custody for the sample is followed until the sample is processed and stored in the GCP Facility.

- In the absence of the GCP Lab technician, (and when delegated, for example during University Closed Days, and when samples are collected out of hours) process and store the Panc Rota samples.

5.1.3 Responsibilities of the GCP Facility Staff:

It is the responsibility of the delegated GCP Lab staff to:

- Ensure that all samples collected are recorded on the LIMS

- Store the tissue samples in the GCP Biobank and record the location of the tissue samples on the LIMS.

- Ensure that the current batch of isopentane used in the sample collection is logged on the LIMS.

- Process and store the Panc Rota samples unless during a University Closed Day (or out of hours) or the task is delegated to a Research Fellow by the GCP Lab Operations Director.

- Ensure that any SOP deviations with respect to the samples are recorded on the LIMS and the Quality Assurance Manager and Operations Director is informed.

5.2 PROCEDURE

5.2.1 Obtaining Informed Consent:

- The research and what is involved in the collection of samples should be discussed with the patient at least one day before the operation. The patient should be taken through the consent process as detailed below.

- Patients who are scheduled to undergo surgery of the pancreas should be given the opportunity to take part in the research programme. It should be an informed, non-coercive discussion in appropriate language that will be understood by the patient.

- Following this, the patient should be given the opportunity to ask questions about the project, understand why the research is being done and any foreseeable risks involved.

- If the Researcher is unable to answer the patient's questions then and answer should be sought from someone qualified to do so.

- The patient should be given ample time to read the Patient Information Sheet relating to the research, which they should keep before the consent form is signed.

- The Researcher should explain to the patient that participation is voluntary and that they may withdraw at any time from the project, without giving any reason and without medical care or legal rights being affected.

- The Researcher should explain to the patient that any of their medical notes may be examined by responsible individuals from the research group or from regulatory authorities (e.g. Local Research Ethics Committee) where it is relevant to their taking part in research.

- The patient should understand that the research group will hold the information collected about them and that the group is registered under the Data Protection Act to hold such information. The research being undertaken has been rigorously reviewed by both MREC and LREC groups and been granted favourable approval (Ref: MREC/03/6/89).

- The patient must understand that their patient data will be stored and used for research purposes.

- If the patient agrees to take part in the project, the following samples will be requested; urine, blood, tissue, pancreatic juice for the research specified by the Researcher. The patient must freely agree before any samples may be taken.

- The patient should understand how the samples will be collected and that giving a sample is voluntary.

- The patient should understand that they are free to withdraw their approval for use of their sample(s) at any time without giving any reason and without their medical care or legal rights being affected. In this case they should understand that any research material relating to them including biological sample(s) would be destroyed in an appropriate fashion.

- The patient must agree to take part in the project and agree to donate their sample (urine, blood, tissue, pancreatic juice) for the research specified by the Researcher and any future research related to diseases of the pancreas carried out within the European Union.

- It should be explained to the patient that research using their donated samples may include research aimed at understanding the genetic influences on pancreatic diseases but the results of these investigations are unlikely to have personal implications for them.

- The participant should be aware that there are no financial benefits if the research leads to the development of new treatments or medical tests.

- **The section on the consent form concerning the version and date of the Patient Information Sheets must be completed by the patient. The participant must initial each specific point in the adjacent boxes on the form and then the patient and Researcher should both sign the consent form.**

- The original signed consent form should be placed in the patient's case notes, a copy should be given to the patient and a copy should be retained by the Researcher and returned to the GCP technician to file in the Pancreas Bank section of the GCP Facility Manual. The delegated Senior Clinical Research Fellow and the GCP Lab OD will audit signed consent forms at the end of each month of duty and the findings will be recorded and kept on file.

- **The time and date of collection should be clearly written on the sample checksheet.**

- **The 'Patient data sheet for pancreatic research' sheet, AND consent form, and checklist should be filled in with all relevant information and left with the blood tubes in the GCP Lab Freezer Room for processing by delegated individual.**

- **The Pancreas Rota collects: Blood (Plasma-EDTA and Serum) and Urine (pre-op), Pancreatic Juice and Tissue Samples for future research.**

5.2.2 Blood Sample Collection:

1. A qualified doctor must receive informed consent from the patient prior to any samples being taken.

2. The Rostered Research Fellow should collect a total of 18ml of blood from the consented patient **prior to anaesthesia:**

    - 9ml in a SARSTEDT Monovette EDTA KE 9ml tube.

    - 9ml in a SARSTEDT Monovette Serum Z 9ml tube.

3. **The sample should not be taken during anaesthetic. If for some reason this is unavoidable then this must be recorded on the worksheet and through the adverse event button on sample reception on the LIMS.**

4. Blood tubes, urine pot, needle, consent form and data sheet are provided in the 'Panc Rota' kit, all non-kit components required for sample collection are available on the ward. The Panc Rota sample collection kit, LTB consent and Patient Information Sheet, and LIVC3 sample collection kit (if required, samples for this study are not routinely collected on a regular basis) should be collected from the GCP facility freezer room or GCP office (Tel: 706 4948).

5.2.3 Urine Sample Collection:

1. A qualified doctor must receive informed consent from the patient before any samples are taken.

2. The Rostered Research Fellow should ask the patient to provide a **preoperative** urine sample of at least 60ml (or as much as the patient can provide up to a full urine pot).

3. **The sample should be collected in the morning before surgery and during fasting. If for any reason urine is taken at another time this must be noted on the worksheet and through the adverse event button on sample reception on the LIMS see section 5.2.7 below.**

4. The urine sample should be left in the pre-labelled urine pot, in the GCP Freezer Room for processing.

5.2.4 Tissue Specimen Collection:

1. A qualified doctor must receive informed consent from the patient prior to any samples being taken.

2. The processor should prepare (in advance) the Tissue Collection Nunc cryovials (NuncT from the 'processing half' of the Panc Rota kit) for the snap freezing of tissue specimens by adding 1ml of isopentane to each. The GCP Technician should maintain the LIMS to ensure that only the current in-use batch of isopentane is recorded on the LIMS.

3. The following NuncT tubes are coded as detailed below:

    - 3 x Trucut (Needle biopsy) – Grey cap
    - 1 x Duodenum – Yellow cap
    - 1 x CBD – Green cap
    - 1 x Pancreas Neck – Red cap
    - 1 x Normal Tissue – White cap
    - 1 x Tumour Tissue – Blue cap

- **Note: If during the operation, a different type of specimen is received other than that denoted by the colour of the tube then one of the following must be done:**
- **Log the samples collected on the LIMS (see section 5.2.6)**
- **Inform the processor if other than the research fellow and record on the checklist**
- **If more tubes other than those provided are required then use the Panc Rota 'E'**
- **If an adverse event with respect to the tissue samples occurs then record this following the instructions in section 5.2.7**

4. When the Research Fellow receives the **first call to theatre,** they should take the pre-labelled (with LIMS labels) NuncT cryovials and the liquid nitrogen flask to the theatre.

5. Once the tumour has been fully mobilized and is believed to be resectable, trucut biopsies of the tumour are usually taken. The tissue should be immediately put in isopentane and the cryovials immediately put into the liquid nitrogen flask (i.e. snap-freezing procedure described below).

    - **Snap-freezing Procedure:**

- Use a sterile pair of forceps to place the right amount of tissue into each Nunc tube containing 1ml of isopentane.
- Close the lid of the Nunc tube and drop gently into the liquid nitrogen container.

6. Store the flask in theatre until the second call to theatre.

7. The Research Fellow will receive the **second call to theatre** immediately prior to the removal of the resected specimen.

8. Whilst waiting for the main specimen it is the responsibility of the researcher to complete the Histopathology forms for *each* specimen pot and to ensure that a copy of the completed LTB Tissue consent form accompanies the main specimen.

9. Any specimens collected should be snap-frozen immediately as described above (6).

10. On receipt of the main resected specimen the Research Fellow should transfer it, in a large, specimen pot containing cold PBS to the tissue processing room in the Department of Pathology, 5th Floor Duncan Building.

11. The Research Fellow will have previously arranged to deliver this specimen and a pathologist will dissect the tissue to isolate the tumour.

12. The Research fellow will then collect the Liquid Nitrogen flask from the LTB and return it to the freezer room for storage, and will inform the person responsible for storing the tissue if different from the Research fellow.

    - If necessary and if staff are available, the LTB may store the tissue overnight at -150°C for subsequent collection or leave in the temporary liquid nitrogen store. In which case it is the responsibility of the GCP technician to ensure this is file noted for that sample.

5.2.5 Paxgene Biopsy:

1. A qualified doctor must receive informed consent from the patient prior to any samples being taken.

2. The GCP Technician should prepare (in advance) the Tissue Collection Paxgene tube (from the 'processing half' of the Panc Rota kit).

3. The following tubes are coded as detailed below:

    - 1 x Paxgene tube

4. When the Research Fellow receives the first call to theatre**,** they should take the pre-labelled (with LIMS labels) Paxgene tube to the theatre.

5. Once the tumour has been fully mobilized and is believed to be resectable, the tissue should be immediately put in the PAXgene tube.

6. Use a sterile pair of forceps to place the right amount of tissue into the Paxgene tube.

7. Store the tube in theatre along with the liquid nitrogen flask until the second call to theatre.

8. The Research Fellow will receive the second call to theatre immediately prior to the removal of the resected specimen.

9. The research fellow should note on the Paxgene Shipment sheet (Appendix 2) providing the time/date of sample collection.

10. The tube will be returned by the Research fellow along with the Liquid Nitrogen flask to the freezer room, and will inform the person responsible for storing the tissue if different from the Research fellow.

5.2.6 Collection of Pancreatic Juice:

1. When the Research Fellow is called to theatre, a sample of Pancreatic Juice may be given.

2. The sample must be transferred to the GCP Freezer room in a plastic bag as soon as possible.

3. The processor (if different) must be informed that the sample is in the GCP Freezer room as soon as possible.

4. The processor should log the reception of the sample on the LIMS (according to **SOP, GCLPTSS048: Processing of Samples for the Pancreas Bank**).

5.2.7 Recording Sample Collection on the LIMS: Confirmation of Samples Taken:

1. Access the LIMS and login according to **SOP: Accessing and Recording Processes on the LIMS**. Select Trials and Studies, from the drop-down menu, select Panc Studies and Panc Rota. The Panc Rota workflows screen will pop up (Figure 1).

Figure 1 **'Panc Rota Workflows'** screen

2. Select the **'Confirm Sample Taken'** icon, the **'Patient ID'** screen will appear (Figure 2). It is essential that the date for the collection of EDTA tube, Serum, Urine and Nunc T (tissue samples) is recorded. Select the kit used to collect the sample, then select the EDTA tube, click on the calendar icon. The calendar screen will pop up (Figure 3), select the date on which the sample was

taken, click on the **'OK'** icon . Repeat for the Serum, Urine (U-Pot) and Nunc T tube (NuncT).

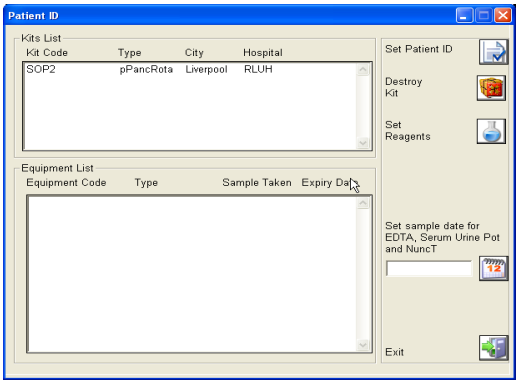

Figure 2 **'Patient ID'** screen

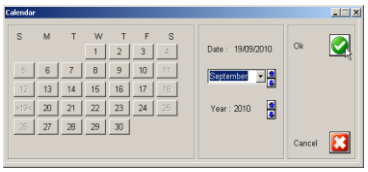

Figure 3 Calendar screen

3. Select the **'Patient ID'** icon ,the 'Fax Received' screen (Figure 4) will appear, the patient ID code should automatically be set (this is the kit code), complete the Consent ID code from the drop-down menu and the Research Fellow who took the sample. Click on the **'Ok'** icon . There should be a return to the 'Patient ID' screen (Figure 2). Click on the **'Exit'** icon .

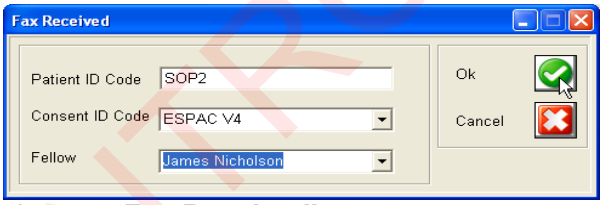

Figure 4 **'Fax Received'** screen

4. Select the **'Tissue (-150 or LN2)'** icon , on the **'Panc Rota Workflows'** screen (shown in Figure 1). The **'Sample Lifecycle'** Pancreas Rota Tissue screen will appear (Figure 5). Select the **'Receive Samples'** icon . The **'Samples Received'** screen will appear (Figure 6).

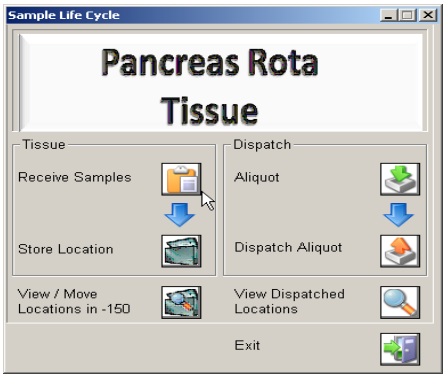

Figure 5 **'Samples Lifecycle'** screen - Pancreas Rota Tissue

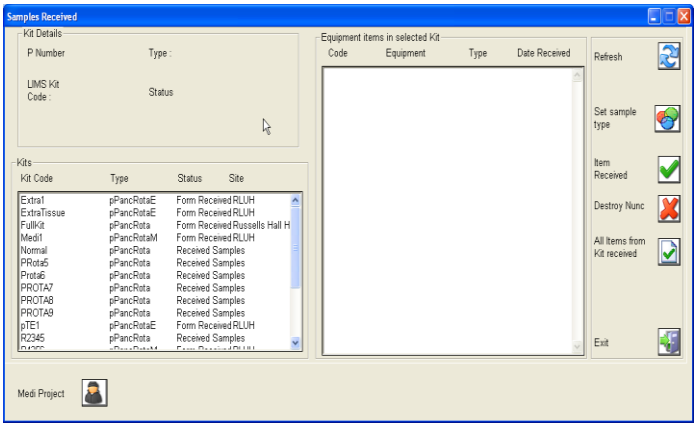

Figure 6 **'Samples Received'** screen

- **If there is an adverse event associated with the tissues collected then this must be recorded on the LIMS as the tissue sample type is set.**

6. Select the kit code and the NuncT tube code containing a tissue sample, select the **'Set sample type'** icon a **'Set Sample Type'** screen (Figure 7) will appear. Select the sample type from the drop-down menu. Add any further information in the description box e.g. Trucut. If the sample type does not appear, select **'Other'** from the drop-down menu, and add the type of sample in the description box. Select the **'Ok'** icon, the screen will return to the **'Samples Received'** screen, with the **'Type'** field populated with the nature of the sample. Select the next NuncT tube and add the sample type.

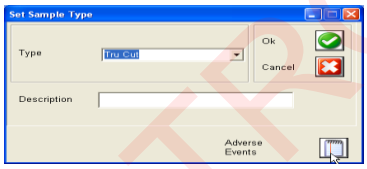

Figure 7 Drop-down menu denoting sample type

7. Once the sample type has been set, the collected samples should be formally recorded as received on the LIMS. If the person recording the sample collection is not the processor i.e. not continuing to physically store the samples in the freezer, then select the **'Exit'** icon, exit the workflows and the LIMS by selecting the icons to close the LIMS screens.

8. The processor (person recording the sample reception when different from the collector) should log in to the LIMS, select '**Trials and Studies'**, select the **'Panc Rota'**, select **'Panc Rota Workflows'** screen (Figure 1), then the **'Tissue (-150 or LN2)'** icon. The **'Sample Life Cycle'** screen will appear (Figure 5) select the **'Receive Samples'** icon. The **'Samples Received'** screen will appear (Figure 8), select the kit (same as the designated patient ID) from the list. The samples collected from that kit will appear as inputted by the collector.

9. Select the individual specimen (Nunc T) select the **'Item Received'** icon ✔ for each sample type, the **'Date Received'** field will be populated with the current date on which the sample is received.

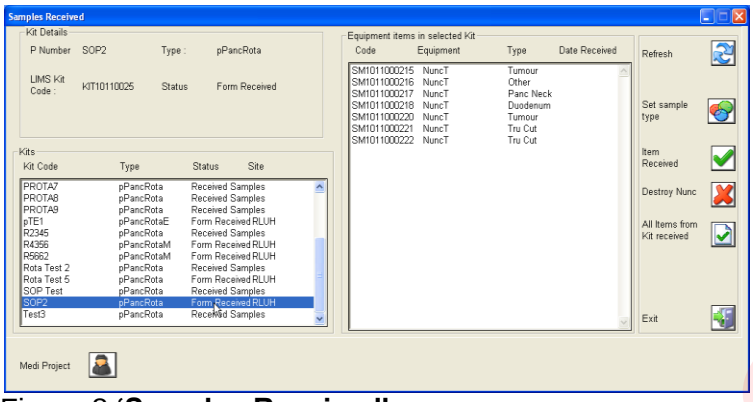

Figure 8 **'Samples Received'** screen

10. A **'Select Reagents'** screen will appear (Figure 9), the isopentane batch used for sample collection must be selected. Select the batch of isopentane and click on the **'Add'** icon ✚ this will add the batch of isopentane to the sample (Figure 10).

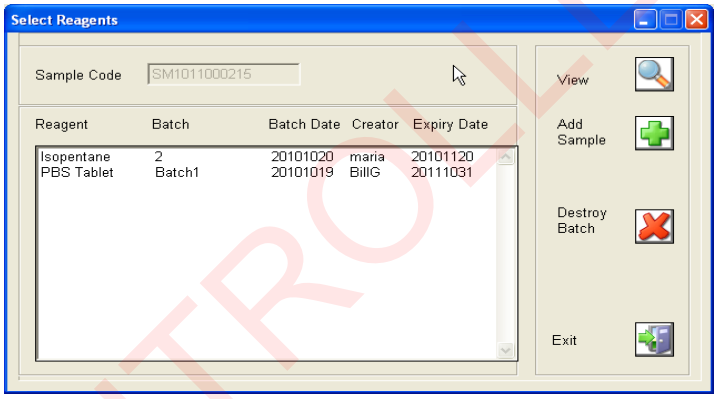

Figure 9 **'Select Reagents'** screen

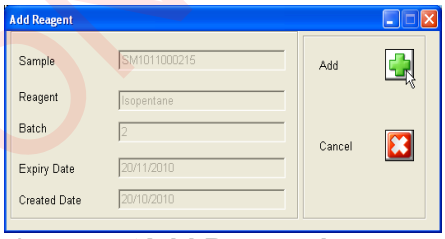

Figure 10 **'Add Reagent'** screen

11. This must be repeated for the batch of PBS used in sample collection. Repeat for all samples as the receipt of each sample is confirmed by selecting each sample and clicking the **'Item Received'** icon ✔.

12. Once all sample types have been confirmed as received, select the **'All Items from Kit received'** icon . Select the **'Exit'** icon and return to the **'Sample Lifecycle'** screen (Figure 5).

13. Select the **'View/ Move Locations in -150'** icon , the **'Sample Location'** screen will appear (Figure 11), search the freezer for the next unoccupied spaces in order to store the received samples. Either filter by freezer or by date received). Select the **'Exit'** icon to return to the **'Sample Lifecycle'** screen (Figure 5).

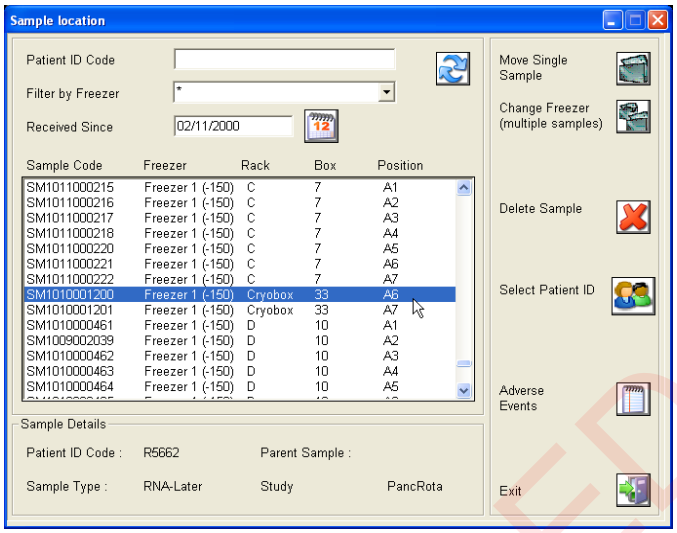

Figure 11 **'Sample Location'** screen

14. Select the **'Store Location'** icon from the **'Sample Lifecycle'** Pancreas Rota Tissue screen (Figure 5), the **'Store Location'** screen will appear (Figure 12). Select the Kit type, and the sample to be stored, select the **'Store location'** icon .

15. The **'Storage Location'** screen will appear (Figure 13), select the Freezer, Tower, Box, and storage position for the sample from the drop-down menu. Select the **'Ok'** icon to confirm the co-ordinates of the sample.

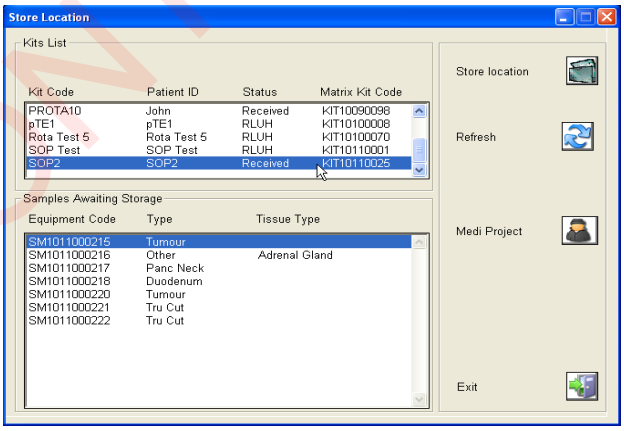

Figure 12 **'Store Location'** screen to select samples by kit code and sample type awaiting storage

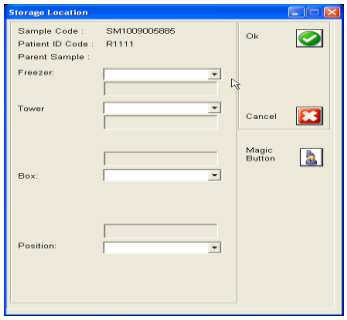

Figure 13 **'Storage Location'** screen

16. The LIMS will return to the **'Store Location'** screen (Figure 12) to log the location of each sample. Select the sample to be stored, select the **'Store location'** icon . The storage location screen will appear, select **the 'Magic Button'** icon . This **'Magic Button'** will populate the storage location screen with the previously logged sample position. To store the current sample change the **'Position'** location to log the final position of the current sample to be stored. Repeat for all tissues to be stored.

16. Select the **'Exit'** icon to return to the **'Sample Lifecycle'** Pancreas Rota Tissue screen (figure 5). When all samples are stored, select **'Exit'** to return to the **'Panc Rota Workflows'** screen. Select **'Exit'** to return to the main screen. Finally click on the icon to leave the LIMS.

6. ABBREVIATIONS

GCLP	Good Clinical Laboratory Practice
LIMS	Laboratory Information Management System
LREC	Local Research Ethics Committee
LTB	Liverpool Tissue Bank
MREC	Multicentre Research Ethics Committee
OD	Operations Director
PBS	Phosphate buffered saline
PI	Principal Investigator
QA	Quality Assurance
SOP	Standard Operating Procedure

7. OTHER RELATED PROCEDURES AND DOCUMENTS

Documents:

GCLPTSS047/F1	Worksheet for the Collection of Samples for the PANC Rota

SOPs:

GCLPRPS011	Use of the LIMS to Record Kit Construction, QC, Storage and Dispatch
GCLPTSS047	Processing of Samples for the Pancreas Bank SOP

8. APPENDIX

8.1 Appendix 1: Example of a Sample Collection Worksheet for the Pancreas Rota

WORKSHEET FOR THE COLLECTION OF SAMPLES FOR THE PANC ROTA

Date consent taken	Consent taken by:	Consent Form Ref:

Pre-Op Sample Collection

Sample Collected by:

Sample Type:	Date collected:	Time collected:	Collected by:
EDTA			
Serum			
Urine			

Specimen Collection during procedure

Sample Collected by: (if different from Pre-op sample collector)	
Time Called to Theatre	
Time Second Call to Theatre	
Time Specimen is excised	
Time Specimens retrieved from Pathology	
Time Specimens Taken to the GCLP Facility	
Time Pancreatic Juice collected	

Specimens Collected (Contents NuncT tubes)

Cap Colour Coded Tube	Sample Type (Tick box if matches code otherwise state tissue collected in NUNC)	
Grey	➢ Trucut ➢ Trucut ➢ Trucut	➢ ➢ ➢
Yellow	Duodenum	
Green	CBD	
Red	Pancreas Neck	
White	Normal	
Blue	Tumour	
No colour (extra tubes)		
No colour (extra tubes)		
No colour (extra tubes)		
No colour (extra tubes)		

No colour (extra tubes)		
No colour (extra tubes)		

Permanent Locations:

Tissue Type	Location (freezer, tower, box, co-ordinate)
	➢

Additional Information/Adverse Events

8.2 Appendix 2: Example of a Paxgene Shipment Sheet

PAXGENE SHIPMENT

Site Name	Royal Liverpool University Hospital	
Kit Number		
Date Sample Taken		Time Sample Taken
__/___/____		__:__
Sample Taken By	PrintName:_____ Signature:_____ Date:__/___/____	
Date Sample Posted		Time Sample Posted
__/___/____		__:__
Sample Posted By	PrintName:_____ Signature:_____ Date:__/___/____	
Date Sample Received		Time Sample Recieved
__/___/____		__:__
Sample Received by	PrintName:_____ Signature:_____ Date:__/___/____	
Comments:		
This form should be completed and e-mailed back on receipt of samples to the Liverpool GCP technician at: gdonegan@liverpool.ac.uk		