	LCTU GCPLab **Standard Operating Procedure** **COLLECTION OF SAMPLES FOR THE CHRONIC PANCREATITIS BIOBANK**		
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1	29/08/2012	13/11/2012	Change in facility name, routine blood test, clarification of nursing names & removal of recruited form	2413
2	11/02/2013	15/01/2016	Grammatical and sentence structure alterations	4443
3	03/03/2016	26/07/2018	Amended PBRU reference to LPRG	8362

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1. WHO?

This Standard Operating Procedure (SOP) applies to all delegated researchers (clinical fellows, research nurses, research assistants, research students, LPRG staff and GCPLab staff) to the Chronic Pancreatitis Biobank who: identify suitable patients, request and obtain informed consent and collect samples from patients for the Chronic Pancreatitis Biobank, located in room 3.3.73 3rd Floor UCD Building, Royal Liverpool University Hospital (RLUH).

2. BACKGROUND

A major activity of the translational work is the collection and storage of human pancreas tissues for future, ethically approved, translational research. This involves the Researchers and GCP Laboratory staff working as a team, to ensure that samples are collected according to GCP principles, legislation, only after full, informed consent is obtained and the rights and well-being of the patient is of paramount importance. The samples should be processed in a timely manner, the chain of custody maintained and the integrity of the sample assured. The samples should be stored to ensure that they can be accessed when needed for ethically approved future work.

Patients admitted to RLUH with provisional diagnosis of Chronic Pancreatitis will be approached to participate in the LPRG Chronic Pancreatitis Biobank project and asked to donate their blood and urine samples to the biobank. These samples will be processed to render into constituent components (plasma, serum, DNA) which will be stored in the Chronic Pancreatitis Biobank. These samples will be used in future projects (following ethical approval) looking at the diagnostic and therapeutic aspects of Chronic Pancreatitis.

3. PURPOSE

The purpose of this SOP is to describe the procedures and processes involved in the taking of informed consent, sample collection and transfer to the laboratory for processing and storage in the Chronic Pancreatitis Biobank.

4. SCOPE

This SOP is to describe the procedure to request informed consent and subsequent safe collection of samples for the Chronic Pancreatitis Biobank located on the 3rd Floor UCD Building, Royal Liverpool University Hospital. This document applies to all staff involved in collecting samples for the Chronic Pancreatitis Biobank.

5. PROCEDURE

5.1 RESPONSIBILITY

- It is the responsibility of those staff delegated (by management) to the Chronic Pancreatitis Biobank: including clinical research fellows (“researcher”), research nurse staff, research assistants, research students, data managers and other clinical staff (when trained and where appropriate) to obtain informed consent and collect samples from patients with chronic pancreatitis.

- It is the responsibility of the research fellow/ "researcher" who is currently delegated to the role by management to identify potential patients who are eligible and who may be approached to give informed consent to donate the samples.
- It is the responsibility of the staff member/researcher in the clinic to ensure that the donated samples are transported to the laboratory intact and safely in order for the samples to be processed and stored.
- It is the responsibility of all staff delegated to the Chronic Pancreatitis Biobank to follow this SOP when consenting patients and collecting the samples.

5.2 PROTOCOL

5.2.1 Risk Assessment:

Hazard: **Biological contaminants in human blood/urine**
Risk: **Possible exposure to the above biological contaminants present in human blood/urine**

Procedures to minimise risk:

- Safety needles must be used at all times.
- Sharps (needles etc.) should be placed directly into the sharps bin – **NO RESHEATHING OF SHARPS**
- Gloves should be worn for venepuncture and collection of samples

5.2.2 Identification of Patients:

For the purpose of this study, any patient with a clearly documented diagnosis of chronic pancreatitis in the notes or clinic letter from one of the pancreatic consultants or directly informed by the patient's clinician from the Professorial Pancreatic clinic will be eligible for inclusion into the study.

In most cases these patients will be identified prior to clinic by the member of staff scheduled to cover that clinic and will be highlighted as a possible candidate for the Biobank. A list of patients attending clinic will be identified from iPM computer system. This will be done by either looking through the case notes, or accessing patient information via the hospital intranet (iPM and ICE). These patients will be cross-referenced with the current database of recruited patients to ensure they have not already donated. This can be found on the PBRU J drive in the PBRU General folder on the Trust computer system, within the folder, Chronic Pancreatitis.

Patients with a clearly documented diagnosis of chronic pancreatitis (i.e. histological confirmation, multiple clinical letters confirming diagnosis from a consultant HPB surgeon) will ideally be initially approached by a researcher while they are waiting for their clinic appointment, and given the Patient information sheet on what would be required for them to donate a sample for the Chronic Pancreatitis Biobank.

The diagnosis of Chronic Pancreatitis will be made as in normal clinical practice, by the clinician in charge of the potential participant's case, taking the following into consideration:

a) Characteristic clinical features of chronic pancreatitis
    - Recurrent abdominal and/or back pain
    - Presence of predisposing factors such as
        - Alcoholic dependence

- Smoking
- Obesity
- Presence of certain genetic mutations
- Hypertriglyceridaemia

b) Pancreatic exocrine insufficiency
   - Evidence of significantly decreased digestive enzyme secretion
     - Quantified faecal fat excess
     - Abnormal faecal elastase (on 2 separate occasions)
     - Decreased output on secretin stimulation test

c) Imaging
   - Imaging indicative of chronic pancreatitis
     - Pancreatic parenchymal calcification
     - Pancreatic ductal abnormality secondary to chronic pancreatitis
   - Characteristic morphological abnormality
   - Ductal calculi
     - EUS criteria
     - Parenchymal features
   - Hyperechogenic foci
   - Hyperechogenic stands
   - Lobulation
   - Cysts/pseudocysts
   - Calcification
     - Ductal features
   - Dilated duct
   - Irregular duct
   - Hyperechogenic ductal margins
   - Visible side branch ducts
     - Pancreatic atrophy

d) Histology
   - Biopsy and/or resection specimen indicative of chronic pancreatitis showing parenchymal damage and fibrosis

5.2.3 Collection of Kits:

Kits will be made GCLP facility or LPRG laboratory. Kits are stored in the LPRG main lab, and will be dispatched prior to sample collection (both physically and on LIMS). Chronic Pancreatitis Blood Kits for the sample collection for Chronic Pancreatitis Biobank, once dispatched are kept in a box which will be held by the individual dedicated to sample collection at that time. This file will be taken to each clinic. There should always be at least 8 kits available for each clinic. Chronic Pancreatitis Blood Kits for laboratory processing for the Chronic Pancreatitis Biobank are kept in the LPRG lab.

The pancreatic clinics are currently held on Tuesday mornings and Wednesday afternoons on the 2nd Floor of the Linda McCartney Centre and on a Monday mornings and Thursday afternoon in clinics J and K on the ground floor of the RLUH building. If they are moved to another time or location then collection can be altered accordingly. Any change in location will be determined by the research fellow and communicated to the collector.

5.2.4 Approaching the Patient:

Usually patients with chronic pancreatitis will be identified in outpatient clinics, but they may also be identified on the ward with an acute attack, or having been admitted with some other problem. The Hepatopancreatobiliary Specialist nurse will alert the Chronic Pancreatitis database holder of any admissions.

These patients must meet the following criteria to be eligible for donating samples to the biobank:

- Patients over the age of 18
- Ability to understand and comprehend the purpose of the sample collection and willingness to enter into the project
- Provisional/confirmed diagnosis of chronic pancreatitis (clinical symptoms and signs suggestive of the disease)

5.2.4.1 Approaching a Patient in Clinic:

The previously identified patient will be initially approached while they are waiting for their appointment and given a brief overview of the project and the participant information sheet to read. A supply of patient information sheets will be kept in the Chronic Pancreatitis box file. If they are not found there, they can be printed off from the University of Liverpool SharePoint Online, Liverpool Pancreatitis Research group folder. As many patients have to travel a long way to attend the clinic they must be given the option of consenting to take part in the study on that occasion, or think about it until their next routine outpatient appointment.

5.2.4.2 Approaching a Newly Identified Patient:

If a patient attends clinic and is only identified as a potential subject for the Biobank at that time, they can be initially approached by the clinician making the diagnosis and then directed to the researcher in clinic for further information.

5.2.4.3 Approaching a Patient on the Ward:

Patients will be identified by the clinician during their inpatient stay or as the patient is already registered on an existing database. They will be initially approached on the ward, given basic information about the project and a copy of the Patient Information Sheet, and then approached again later to see if they are happy to go through the formal consenting process for the study.

5.2.5 Consenting the Patient:

Prior to talking to the patient, the person delegated to collect the sample, should ensure they have the relevant consent version and patient information sheet as approved by the REC committee.

After formal introduction, the nature of the biobank should be explained in great detail to the potential participant. This should also include diagrams if needs be to explain the nature of the biobank and what it aims to achieve.

The salient features of the consent process are:

- It should be informed, non-coercive discussion in appropriate language that will be understood by the patient.

- The researcher should explain and emphasize that the 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 Ethic Committee) where it is relevant to their taking part in the research.

- The patient should understand that the research group will hold information collected about them and that the group is registered under Data Protection Act to hold such information.

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

- The patient must agree to take part in the project and agree to donate their blood, urine or sample of pancreatic juice for the project.

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

- It should be explained to the patient that the project is aimed at understanding genetic influences on pancreatic diseases but the results of these investigations are unlikely to have personal implications for them.

- They give permission for their anonymised results to be published, including genetic information.

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

- The patient should understand that they are free to withdraw their approval for use of their sample(s) at any time (whether it is shortly after donating the sample or far later after the donation) without giving any reason and without their medical care and legal rights being affected. Should they decide to withdraw their sample long after the donation they should contact the appropriate person name on the patient information sheet. They will contact the appropriate member on the team who will follow correct procedure to withdraw a patient's sample. The donor should understand that any research material relating to them including biological sample(s) would be destroyed in an appropriate fashion according to SOPs and in line with NHS Policy if possible.

- Following this this discussion, 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 any of the patient's questions, then an answer should be sought from someone qualified to do so.

- The patient should then be given the Participant Information Sheet relating to the project to read which they should read and keep before the consent form is signed.

- The participant should be given adequate time to think about the information given and read the participant information sheet and ask further questions if needs be to clarify their queries.

- Once the participant has agreed to donate to the biobank, the consent form should be signed.

- The patient and researcher should sign both sides of the consent form. The participant should initial each specific point in the adjacent boxes on the form.

The signed consent form should be photocopied, one copy to be kept in the patient's notes, another to be given to the patient and the original to be kept in the folder 'Consent Form for the Chronic Pancreatitis Biobank Sample Collection' which is kept in Room 3.301 located on the 3rd Floor UCD Building, RLUH.

If the patient is deemed too unwell to understand or comprehend the information and is incapable of making a decision, it is not appropriate to take a sample from that patient at that time.

5.2.6 Sample Collection:

5.2.6.1 Urine Collection:

- Provide the patient with the sample collection pot for urine from the kit. If patients cannot provide the sample at that time, if they are an inpatient leave it with them and collect it after 2 hours. If they are catheterized, obtain the sample directly from the catheter bag (approximately 15ml)

5.2.6.2 Blood Collection:

- **If it is appropriate to perform phlebotomy before the patient has been seen by a clinician** it is appropriate to take routine bloods at the same time as taking the blood samples for the Chronic Pancreatitis Biobank. The tests that would be counted as "routine bloods" for patients with chronic pancreatitis are: Full Blood Count, Urea and Electrolytes (including an Estimated Glomerular Filtration Rate), Liver Function Tests, Calcium profile, magnesium, vitamin D, inorganic phosphate, Ca 19-9 and HbA1C. If the researcher is happy to do this then these bloods may be taken at the same time as the research bloods. Care must be taken to label them appropriately and dispatch to the normal pathology laboratory for processing within the hospital system. Note that the research EDTA and Serum tubes should not be labelled as the sample should be anonymous in the laboratory. If the routine bloods are taken, then a note is written or a sticker stuck in the notes to indicate to the clinician that this has been done.

- **If phlebotomy services are readily available in the clinic and the patient is due to have** routine blood performed, then give the kit to the phlebotomy services to carry out the blood sampling at this time to avoid two venepunctures on the same patient.

- Once the samples have been taken, they are either taken by the researcher to the lab, or the technician is called down to clinic if available to collect the sample for processing.

- **If no phlebotomy services are available** or the patient is being approached on the ward then the researcher must carry out their own venepuncture as described below:

  Make sure you have the kit, consent form (with unique ID on the top) and Patient Information Sheet with you.

  Make sure you have the following (available on the ward):
  - Sharps bin with sample collection tray
  - Blood sample kit
  - Gauzes (available in the clinical utility of the ward)
  - Steriwipes (available in the clinical utility of the ward)

- In the first instance, approach the patient with the consent from and the information leaflet only. Leave the sample collection tray (including the kit) in the clinical utility area (specific to each ward), so that the patient does not feel the pressure to donate the samples. Once the informed consent is obtained, get the sample collection tray from the clinical utility room and proceed.
- Choose the most appropriate peripheral vein and clean it with steriwipe. Using the SARSTEDT Monovette blood taking apparatuses in the kit, perform the venepuncture with the serum tub attached. Once this has stopped filling remove the tube and then attach the EDTA tube. Collect the tubes in the following order:

  1. SARSTEDT Monovette Serum Z (9ml)
  2. SARSTEDT Monovette EDTA K2 (9ml)

- Allow at least 10 seconds for a complete blood draw to take place. Ensure that the blood has stopped flowing into the tube before removing the tube from the holder.

- If any clinical bloods are to be taken at this time then proceed to fill the appropriate tubes.

- The needle should then be removed and venepuncture site covered with gauze (available in the clinical utility room of the ward).

- The needle should be disposed of in the sharps bin.

- Immediately after blood collection, gently invert the tubes 8-10 times.

- Complete the check list for sample collection.

- The samples are then taken to the LPRG Laboratory on the 3rd Floor, UCD Building, and RLUH for further processing.

5.2.7 Sample Delivery:

Once samples have been taken from the patient, they should be processed within 3 hours. Therefore at a convenient time the samples should be taken to the LPRG Laboratory (room 3.302, 3rd Floor of the UCD Building, RLUH) to handover to the member of staff dedicated to processing samples that day. If it will be difficult to ensure that the sample will be delivered to the LPRG laboratory within 3 hours, then the member of staff dedicated to processing should be contacted and asked if they are able to retrieve the sample from the clinical area.

All new patients should be added to the Chronic Pancreatitis database on the PBRU J drive containing the Chronic Pancreatitis research folder on the Trust computer system. Once this is done, all paperwork should be filed in the filing cabinet in office 3.301 on the 3rd Floor of the UCD Building, RLUH, in the relevant file.

6. ABBREVIATIONS

DNA	Deoxyribonucleic acid
EUS	Endoscopic Ultrasound
EDTA	Ethylene-diamine-tetra-acetic acid
ERCP	Endoscopic retrograde cholangiopancreatography
ID	Identification Number
ICE	Integrated Clinical Environment
iPM	i.Patient Manager
LEDDU	Liverpool Early Drug Development Unit
LIMS	Laboratory Information Management System
ml	Millilitres
PBRU	Liverpool NIHR Pancreas Biomedical Research Unit
LPRG	Liverpool Pancreatitis Research group
RLUH	Royal Liverpool University Hospital
SOP	Standard Operating Procedure
GCP	Good Clinical Practice
GCLP	Good Clinical Laboratory Practice
HTA	Human Tissue Act
UCD	University Clinical Department
NHS	National Health Service

7. OTHER RELATED PROCEDURES AND DOCUMENTS

SOPs:

GCLPRPS004	Disposal of Hazardous Waste
GCLPRPS024	Disposal of Hazardous Waste in the PBRU

Policy Document:
PBRU Biobank Policy and Ethical Approval for the PBRU Chronic Pancreatitis Biobank

8. APPENDIX

8.1 Appendix 1: Example of Chronic Pancreatitis Biobank Sample Processing Worksheet

Date _____ **CP____**

CP Processing Worksheet

Consent taken by _____

Processing carried out by _____

	Time taken	Time processing started
Serum		
EDTA		
Urine		

Urine pH pre Tris	
Amount of Tris added	
pH after Tris	
Final pH if further adjusted	

	Number of tubes stored	Freezer	Rack	Box	Position
Serum					
Plasma					
Cell Pellet					
Urine Cryovials					
Urine T					

Please note down any problems with processing-