University of Liverpool GCP Laboratories GCPLab

Collection of Samples for the LPRG Acute Pancreatitis Biobanl

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Author	Latawiec, Diane
Owner	Oates, Mel

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1	13/6/2014	22/12/2015	New Kits included and retrospective consent amended	4318
2	20/05/2016	08/08/2018	Reference to PBRU amended to LPRG and author changed	8360
3	24/08/2018	27/04/2020	Addition to section 5.2 to minimise risk & emphasised that it must be Only clinically diagnosed patients that are approached	11117

CONTENTS

1 WHO?

This Standard Operating Procedure (SOP) applies to all staff that request and obtain informed consent, or retrospective informed consent and collect samples from patients for the Acute Pancreatitis Biobank, which are physically located in GCP Facility, -80 'C freezer, William Henry Duncan (WHD) Building.

2 BACKGROUND

Samples (blood and urine) for the Acute Pancreatitis Biobank will be obtained from patients presenting at RLUH **ONLY** with a diagnosis of Acute Pancreatitis. Patients will be identified through the Biochemistry department who will generate a list of all patients admitted in the last 24 hours with an amylase of >450 U/l at the time of admission. These patients will then be approached for consent. Initial contact will be made by a research fellow or nurse on the study delegation log who will explain in detail, to the patient, the purpose of the biobank, the process of recruitment and various issues surrounding it. If the research fellow or nurse deems the patient to lack capacity to consent, they will make every effort to approach the stated next of kin and ask them to act as consultee for the patient. Capacity to consent will be re-evaluated before every subsequent time point and the patients consent sought whenever they regain capacity.

3 PURPOSE

This SOP applies to all staff involved in obtaining informed consent and collecting samples for the LPRG Acute Pancreatitis Biobank.

4 SCOPE

The purpose of this SOP is to describe the procedure to request informed consent and subsequent safe collection of samples for the Acute Pancreatitis Biobank located in the WHD building GCP facility. This document applies to all staff involved in collecting samples for the LPRG Acute Pancreatitis Biobank.

5 PROCEDURE

5.1 RESPONSIBILITY

It is the responsibility of all clinical fellows, research nurse staff and staff on the delegation log assigned to obtaining informed consent/retrospective informed consent and consultee consent and collecting samples from patients with acute pancreatitis to follow this SOP and any other SOPs pertaining to this assigned role precisely. This will ensure hazards and risks associated with this protocol will be minimized.

5.2 PROTOCOL

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

Procedures to Minimise Risk:

- Sharps (needles etc.) should be placed directly into the sharps bins; **NO RESHEATHING of SHARPS**
- Gloves to be worn for venepuncture and collection of samples.
- ONLY clinically diagnosed acute pancreatitic patients will be approached for recruitment to the biobank.

Equipment needed:

- Sharps bin
- Sample collection kit (Kit A, B, C)
- Cotton wool
- Tape

5.2.1 Identification of Patients:

Patients admitted to the Accident and Emergency Department (A+E) or referred from their General Practitioner with abdominal pain will usually have amylase levels checked to confirm or rule out acute pancreatitis. These results are available through Clinical Biochemistry, RLUH. One of the diagnostic features of acute pancreatitis is a raised level of amylase in blood. All laboratories have different ranges. For the FLUH Clinical Biochemistry Department, the reference range of amylase is: <150 U/I. This range for amylase is used by the recruiter for potential recruitment of patients to the acute pancreatitis biobank. Patients who have raised amylase levels and/or patients highlighted by clinicians who deem a patient to have a working diagnosis of pancreatitis only will be approached for recruitment to the biobank. No patients with other additional clinical diagnosis should be approached.

The amylase list is located on ICE; access to this list is provided during training (GCLPFAC008 – Training of Staff on the Acute Pancreatitis Biobank Rota). The list contains the name of the patient(s), their hospital number, date of birth, place where sample was sent from (A&E/ESAU/Wards), time sample was received and the amylase level.

The list is generated every morning by 0930hrs and should be repeated at 1500hrs to ensure that all patients are captured and sampled within 24hrs of their hospital admission.

If there are any suitable patients on the list, the LPRG staff member responsible for processing patient samples that day should be contacted.

5.2.2 Generation of an Episode Number (AP number):

Once a patient(s) has been identified, they are given an AP number (AP_ _ _). This number is an individual episode of disease onset and does not represent a unique patient. This number is generated by looking through the previous consent forms and taking the next number in sequence. The consent form folder is located in a file, next to the site file for the AP biobank, 2nd Floor Sherrington building 2/025 Room 219

Make a note of the AP number on the top of the consent form and worksheet. All information stored for that particular patient (in the clinical acute pancreatitis database and LIMS system) and future samples collected will be with reference to this specific AP number.

5.2.3 Collection of Kits:

Kits for the samples collection for LPRG Acute Pancreatitis Biobank are kept in 2nd Floor Sherrington building 2/025 Room 219

It is the responsibility of the person collecting the samples to make sure that the correct kit is selected.

Also make sure that a 'Spares Kit' is carried in case any component parts are required.

Check that the kit contains the following pre-labelled tubes:

- **Kit A (24hrs) contains:**
  - BD Vacutainer® Safety-Lok™ Blood Collection Set
  - PAXgene Blood RNA Tube (BRT) 2.5ml
  - BD Vacutainer® K2 EDTA Tube (purple top) 10ml
  - BD Vacutainer® K2 EDTA Tube (purple top) 4ml
  - BD Vacutainer® SST™ Tube (golden top) 3.5ml
  - Sample Processing Checklist
  - Patient information sheet
  - Consent form

- **Kit B (48hrs and weekly) contains:**
  - BD Vacutainer® Safety-Lok™ Blood Collection Set
  - PAXgene Blood RNA Tube
  - BD Vacutainer® K2 EDTA Tube (purple top) 10ml
  - BD Vacutainer® K2 EDTA Tube (purple top) 4ml
  - BD Vacutainer® SST™ Tube (golden top) 3.5ml
  - Sample Processing Checklist

- **Kit C (Referral kit) contains:**
  - BD Vacutainer® Safety-Lok™ Blood Collection Set
  - BD Vacutainer® K2 EDTA Tube (purple top) 10ml
  - BD Vacutainer® K2 EDTA Tube (purple top) 4ml
  - BD Vacutainer® SST™ Tube (golden top) 3.5ml
  - Sample Processing Checklist
  - Consent form

- **The 'Spares Kit' contains:**
  - BD Vacutainer® Safety-Lok™ Blood Collection Set x 3
  - PAXgene Blood RNA Tube x 3
  - BD Vacutainer® K2 EDTA Tube (purple top) 10ml x 3
  - BD Vacutainer® K2 EDTA Tube (purple top) 4ml x 3
  - BD Vacutainer® SST™ Tube (golden top) 3.5ml x 3

Table for LPRG Acute Pancreatitis biobank sample collection:

	24 hours samples	48 hours samples	Week 1 samples	Week 2 samples	Week 4 samples	Referral samples
Kit Type	A	B	B	B	B	C
Plasma and Cell Pellets	14 ml	14 ml	14 ml	14 ml	14 ml	14 ml
Serum	3.5 ml	3.5 ml	3.5 ml	3.5 ml	3.5 ml	3.5 ml
RNA	2.5 ml	2.5 ml	2.5 ml	2.5 ml	2.5 ml	X
Urine	15 ml	X	X	X	X	X

It is the responsibility of the person finishing the rota AND the person commencing the rota for a particular day/week to make sure that they hand over details for patients needing 48hrs/weekly samples efficiently.

Once handed over, it is the responsibility of the person collecting the samples to make sure that it is followed through. Patients requiring 48hrs or weekly samples will not need screening for inclusion or consenting again.

However, cases of Post ERCP pancreatitis need regular clinical evaluation to assess whether they have developed pancreatitis or not. For these patients, the 24hrs samples are collected within 24hrs from the ERCP took place. If their symptoms have lasted for less than 24hrs and their liver enzyme levels have settled/improved, they are not classified as acute pancreatitis and therefore, no further samples are collected. But if their symptoms persist, their 48hrs and then weekly samples are collected as for the other patients.

Patient referred from other hospitals and transferred to RLUH later than 24hrs of initial hospital admission have samples collected in Kit C. These patients will only have one sample taken during their entire hospital admission; therefore, care should be taken to approach these patients. It is therefore advisable to consent them once they are on the ward and able to comprehend the information provided to them. Since these patients need not be captured at any specific time points, retrospective consent should not be sought for them.

5.2.4 Approaching the Patient:

- Make sure you have the correct kit (with the unique ID on the top).
- Once in the ward, patient's clinical notes, blood results and previous reports need to be checked to make sure they meet the inclusion criteria. This is;

  - Patient over the age of 18.
  - Ability to understand and comprehend the purpose of the sample collection and willingness to enter into the project.
  - Provisional working diagnosis only of acute pancreatitis (clinical symptoms and signs suggestive of the disease, amylase of >150 U/I or CT findings correlating with the same).

- Adequate exclusion of other differentials (perforated duodenal/gastric ulcer, acute or acute on chronic liver disease etc.).

- If all of the inclusion criteria are met **apart from** the ability to understand and comprehend the purpose of the sample collection, the next of kin (personal consultee) as stated in the patients' clinical records or a nominated consultee maybe consulted instead for taking informed consent.

- If the patient is deemed to be suitable for the project, make sure you have the following on the sample collection tray (available on the wards):

  - Sharps bin.
  - Kit A/B/C
  - Gauzes (available in the clinical utility of the ward).
  - Steriwipes (available in the clinical utility of the ward).
  - Sample collection pot for urine (available in the clinical utility of the ward).
  - Disposable tourniquet.

- In the first instance, on approaching the patient, first leave the sample collection tray (including the kit) in the clinical utility area (specific to each ward), so that the patient does not feel pressure to donate the samples. Only once the informed consent has been obtained, one can get the sample collection tray from the clinical utility room and proceed.

  If the patient does not meet the inclusion criteria, the reason must be noted down for records.

5.2.5 Consenting the Patient:

After formal introduction, first explain to the patient about the nature of the project and the need for the sample collection.

The salient features of the consenting process are:

- It must be an informed, non-coercive discussion in an appropriate language that will be understood by the patient.
- Following this, the patient must 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 Patient Information Sheet relating to the project to read and digest in a timely manner and which they should keep before the consent form is signed.
- 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 Ethics Committee) where it is relevant to their taking part in 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 and urine sample for the project.
- The patient should understand how the samples are to be collected and that giving a sample is purely 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 and 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 according to SOPs and in line with NHS Policy if possible.
- The patient must agree to take part in the project and agree to donate their blood sample for the research specified by the researcher.
- 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.
- The patient should be aware that there are no financial benefits if the research leads to development of new treatments or medical tests.
- The patient must be given sufficient time to think through the implications of donating a sample, the time needed is entirely the patient's prerogative.
- The patient and researcher should sign both the sides of the consent form. The participant should initial each specific point in the adjacent boxes on the form.

Once the patient has agreed to participate in the project and signed the consent form, it 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 Forms for the Acute Pancreatitis Biobank Sample Collection' kept in the Drawer 1 of the filing cabinet of the Office 2, located on the 3rd floor UCD building.

If the patient is too unwell to understand or comprehend the information and is incapable of making informed consent (but had no problems prior to current admission), their next of kin/ or a nominated individual should be contacted and the same process applied as above, using the 'Personal/nominated consultee Information Sheet' and 'Personal/nominated Consultee Declaration Form' instead of the patient versions. It should be made clear to the consultee that they are expressing an opinion on whether they think the patient would object to participating in the study rather than giving consent on the patient's behalf. A patient's capacity to consent needs to be re-evaluated at every further contact and prior to every further sample collection, and consent sought and recorded as above when the patient regains capacity to make an informed decision, using the patient regaining capacity consent form.

If a patient decides to withdraw consent or withdraws consent after a positive consultee declaration was obtained, the destruction of the sample must be reported on Q-Pulse in accordance with procedure as stated in GCLPFAC014. The sample should then be disposed of according to protocol as stated in GCLPRPS004,

Proceed to the sample collection.

5.2.6 Sample Collection:

For Urine Collection:

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

For Blood Collection:

- Choose the most appropriate peripheral vein and clean it with steriwipe. Using a BD Vacutainer® Safety-Lok™ Blood Collection Set (provided with the kit) perform the venepuncture. Upon getting the blood 'flashback', the blood tubes should be attached to the Luer container one by one replacing each tube when the previous one has been filled, i.e. when the blood stops flowing into the tube. Collect the tubes in the following order:

    1. **BD Vacutainer® K2 EDTA Tube (purple top) 10ml**
    2. **PAXgene BRT RNA Tube 2.5ml**
    3. **BD Vacutainer® SST™ Tube (golden top) 3.5ml**
    4. **BD Vacutainer® K2 EDTA Tube (purple top) 4ml**
    5. **BD Sodium Citrate Tube (blue top) 4.5 ml – (kits P and Q only)**

- Hold the PAXgene BRT vertically, below the blood donor's arm, during blood collection.
- Ensure that the blood has stopped flowing into the tube before removing the tube from the holder.
- The needle is then removed and venepuncture site is covered with gauze (available in the clinical utility room of the ward).
- The needle is disposed of in the sharps bin.
- Immediately after blood collection, gently invert the EDTA (10ml and 4ml) and SST vacutainer® tubes and the PAXgene Blood RNA tube 10 times.
- Complete the check list for sample collection.
- The samples are then taken to the GCP facility (WHD) for further processing.

Samples should be delivered to the laboratory as soon as possible, but no later than 25 minutes.

6 ABBREVIATIONS

A&E	Accident and Emergency Department
BRT	Blood RNA Tube
CAS	Casualty
CT	Computerised Tomography
EDTA	Ethylene-diamine-tetra-acetic acid
ERCP	Endoscopic Retrograde Cholangiopancreatography
ID	Identification Number
LPRG	Liverpool Pancreatitis Research Group

LIMS	Laboratory Information Management Systems
ml	Millilitres
RLUH	Royal Liverpool University Hospital
SOP	Standard Operating Procedure
SST	Serum Separator Tubes
GCP	Good Clinical Laboratory Practice
MHRA	Medicines and Healthcare Products Regulation Agency
HTA	Human Tissue Act
WHD	William Henry Duncan Building
Q Pulse DMS	Q Pulse Document Management System

7 OTHER RELATED PROCEDURES AND DOCUMENTS

SOPs:

GCLPFAC008	Training of Staff on the Acute Pancreatitis Biobank Rota
GCLPTSS049	Processing of Samples for the PBRU Acute Pancreatitis Biobank
GCLPRPS004	Disposal of Hazardous Waste
GCLPFAC014	Recording Quality Incidents and sample destruction on the Q Pulse Management System

8 TRAINING AND RESOURCES

All staff consenting patients and collecting samples must undergo GCP training, as shown on the training log. Training SOP, appropriate training for the Consenting of Patients, collection and processing of samples will be provided by qualified staff. Nursing staff will undertake venepuncture training provided by the Trust along with any other staff that requires phlebotomy training.

9 MONITORING AND AUDIT

Regular audits will be performed to ensure that the protocol in this SOP is followed and samples are appropriately stored. These records will be monitored and audited both internally (Human Materials Governance team) and externally (MHRA inspections) in accordance with the Human Tissue Act (HTA). **Records will be maintained of the fate of all material derived from a patient's samples**

10 APPENDIX

10.1 Appendix 1: Example of Acute Pancreatitis Biobank Sample Processing Checklist

SAMPLE COLLECTION

Person Processing Sample:	**Date:**	**Time:**

KIT CODE:				**PATIENT CODE (AP NUMBER):**
KIT TYPE (tick box)	**A**		**B**	
	C			

CONSENT (tick box and date)				
Consent Obtained	**No**		**Yes**	
Personal/Nominated Consultee Contacted	**No**		**Yes**	

Sample Time Point: (tick box, or complete week number)	
24 hour	
48 hour	
Week No:	

Blood Collected (tick box)		**Time Taken:**	**Tick when each tube is inverted 10 times:**
EDTA Vacutainer (purple top) 10ml			
EDTA Vacutainer (purple top) 4ml			
Serum Tube (golden top)			
PAXgene tube			

Urine Collected	**Amount (ml):**
	Time:
	Date: