Viral Hepatitis Clinical Research Program

Local Laboratory Manual

Laboratory instructions for the collection, processing and storage of study research samples for the studies conducted by Viral Hepatitis Clinical Research Program, Kirby Institute

Coordinating Centre:
Kirby Institute
UNSW Australia
Wallace Wurth Building
Sydney NSW 2052
Australia

For all protocol, study or site management related questions, please contact the study specific Project Coordinator.

This manual is complementary to the protocol and is intended to provide a comprehensive resource to help investigational sites with the conduct of VHCRP studies.

The manual contains general guidelines on study procedures such as handling of clinical supplies and managing study documentation.

Study specific contacts, procedures and guidelines are provided in a study specific supplement.

At any time, if you have difficulty with a procedure contact the study specific Project Coordinator for assistance.

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1. Glossary and Definitions

For the purpose of this study the following definitions will be used:

Table 1: Glossary

ACD	Acid Citrate Dextrose
BSL	Baseline
Central Laboratory	Kirby Institute Laboratory, Sydney Australia
DBS Samples	Dried Blood Spot samples
EDTA	Ethylenediaminetetraacetic acid
ETR	End of Treatment Response
FU	Follow-up
LabKey Offsite Repository	VHCRP's online sample repository database
Participant ID	Unique 11 or 12 digit participant identifier assigned to each participant. The Participant ID contains the protocol number (4 digits)– site number (5 digits)– participant number (2 digits or 3 digits depending on the study size) e.g. 1309-61200-01 or 1309-61200-022
PBMC	Peripheral Blood Mononuclear Cells
PL	Plasma
Research Samples	Processed samples stored for testing and future research including EDTA plasma, EDTA whole blood and PBMCs specimens
RFU	Reinfection follow up
Screening ID	Unique 6 digit participant identifier assigned to a participant at screening. The Screening ID contains a study specific number (3 digits) - participant screening number (3 digits) e.g. 999-001
Site Study Coordinator	Research nurse or coordinator at the site
SOC Samples	Standard of care samples for participant monitoring. Performed at the local site laboratory
Specimen	Biological material collected from a study participant, which will later be processed into research samples. Samples are derived from participant specimens following processing.
Project Coordinator	Kirby Institute Project Coordinator
SST	Serum Separator Tube
SVR	Sustained Virological Response
Term	Termination
VHCRP	Viral Hepatitis Clinical Research Program at the Kirby Institute
WB	Whole blood
WK	Week

2. Communication and Contacts

Protocol enquiries:
For study specific laboratory questions contact the Kirby Institute Project Coordinator. Refer to the study protocol for contact details.

Laboratory enquiries
For general **Laboratory** questions contact the VHCRP Laboratory Coordinator at:

Ph: +61 2 9385 0203 or
Email: HepBank@kirby.unsw.edu.au

3. Specimen Collection and Sample Processing and Storage Overview

Figure 1 outlines the steps involved in specimen collection, sample processing, storage and shipping. Details of each step will follow in the section specified in the diagram.

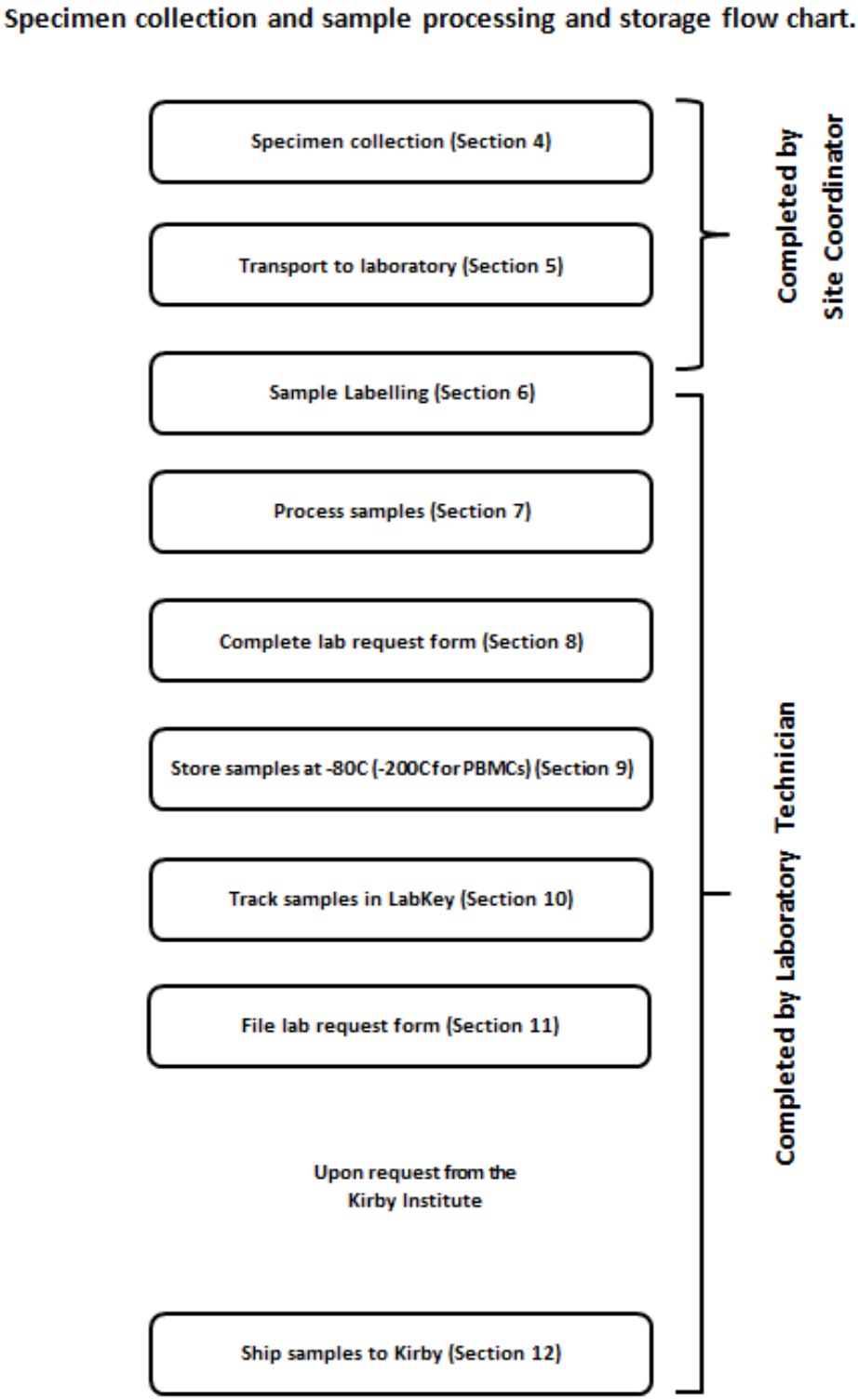


Figure 1: Sample Collection, Processing and Storage Overview

4. Specimen Collection Time Points

All specimens will be collected in the laboratory kits provided to the Site Study Coordinator. Specimens are collected at various time points prior to treatment, through treatment and during follow-up. Samples will be used for central diagnostic testing and will be stored for future hepatitis C related research.

Please refer to section 3: Laboratory Kits of the ***study specific supplement*** for information on the samples types and time points to be collected.

Screening kits are labelled with a screening ID number starting with 3 numbers that are specific to each study (e.g. 999). These kits must only be used for screening visits. If a patient is eligible and is enrolled in the study they will be assigned a participant ID by the Site Study Coordinator at the Baseline visit.

Depending on the study each kit (except the screening kit) may be labelled for a specific participant and a specific visit. In other studies with large participant numbers kits may be generic i.e. not specific to a participant or a study visit. Please refer to your ***study specific supplement*** for specifics as to study kit labelling.

5. Transport of Specimens to Laboratory

The Site Coordinator will be responsible for delivery of samples to the laboratory but the method of transport of specimens to the laboratory will vary between sites. Specimens must be transported safely and securely and in a timely manner.

If problems arise with the transport of samples please contact the Site Study Coordinator immediately.

Please refer to the ***study specific supplement*** for information with regards to site or study specific transport requirements.

6. Sample Labelling

A. Blood Collection Tube Labelling

All blood collection tubes should be labelled by the Site Study Coordinator.

Note: There are three types of specimen labels (See figures 2a, 2b and 2c below);

a) Screening - the participant is given a Screening ID (XXX-screening number)
b) Other Visits (please refer to section 2: Specimen collection time points of the ***study specific supplement*** – the participant is identified by the Participant ID (Protocol number-Site number-participant number).
c) DBS specimen labels

The following visit and participant details should be on the specimen label:

- Patient ID (or Screening ID at screening visits)
- Patient Initials (first two letters of Last Name, first two letters of First Name e.g. Smith, John = SM-JO)
- Date of Birth (DOB) (DD/MMM/YYYY)
- Date of Collection (DD/MMM/YYYY)
- Time of collection (except for DBS collection)

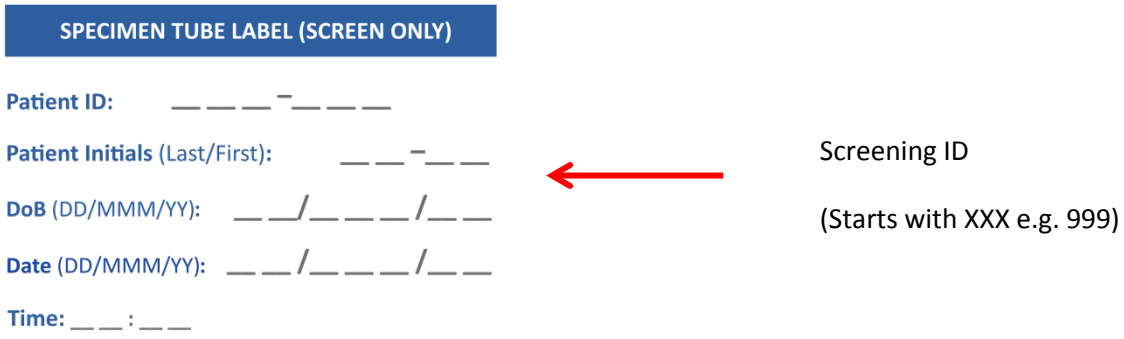
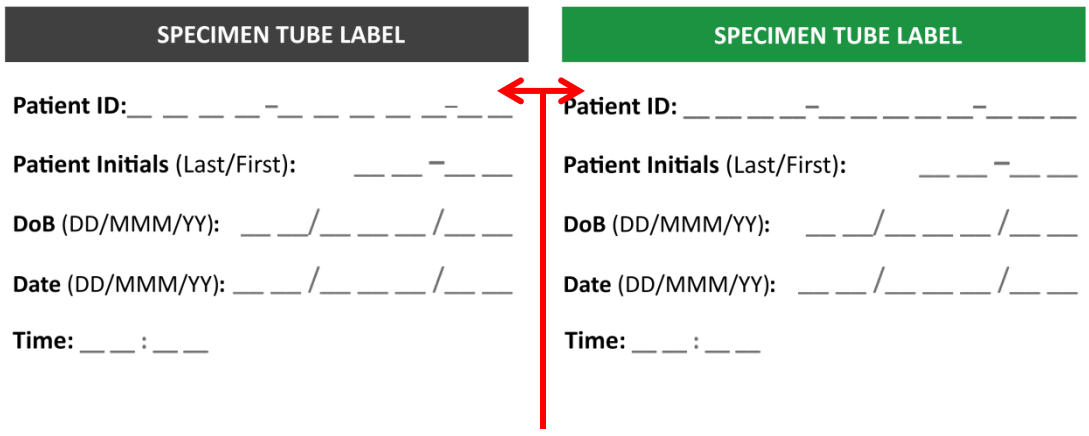


Figure 2a: Screening visit specimen label



Patient ID: (Starts with protocol number, e.g. 1509 – will be used for all remaining visits)

Figure 2b: Other visit specimen label (11 digit Patient ID version (left) and 12 digit Patient ID version (right)

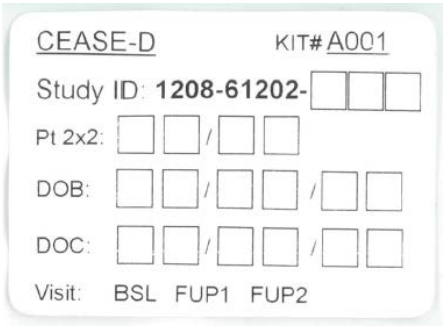


Figure 2c: Dried Blood Spot Label

Please refer to the ***study specific supplement*** for information about study specific labelling requirements.

B. **Aliquot Labelling**

Once a specimen has been collected from a participant, aliquot samples may be processed from these specimens for laboratory testing. Specimens can be processed to produce (but not limited to) the following aliquots depending on the study protocol requirements: EDTA plasma, EDTA whole blood, ACD Plasma, PBMCs or EDTA buffy coat.

The aliquot labels have three very important pieces of information which must be handwritten on them as detailed in Figure 3. It is imperative that the correct aliquot label is placed on each aliquot.

- Participant ID
- Visit name
- Sample type

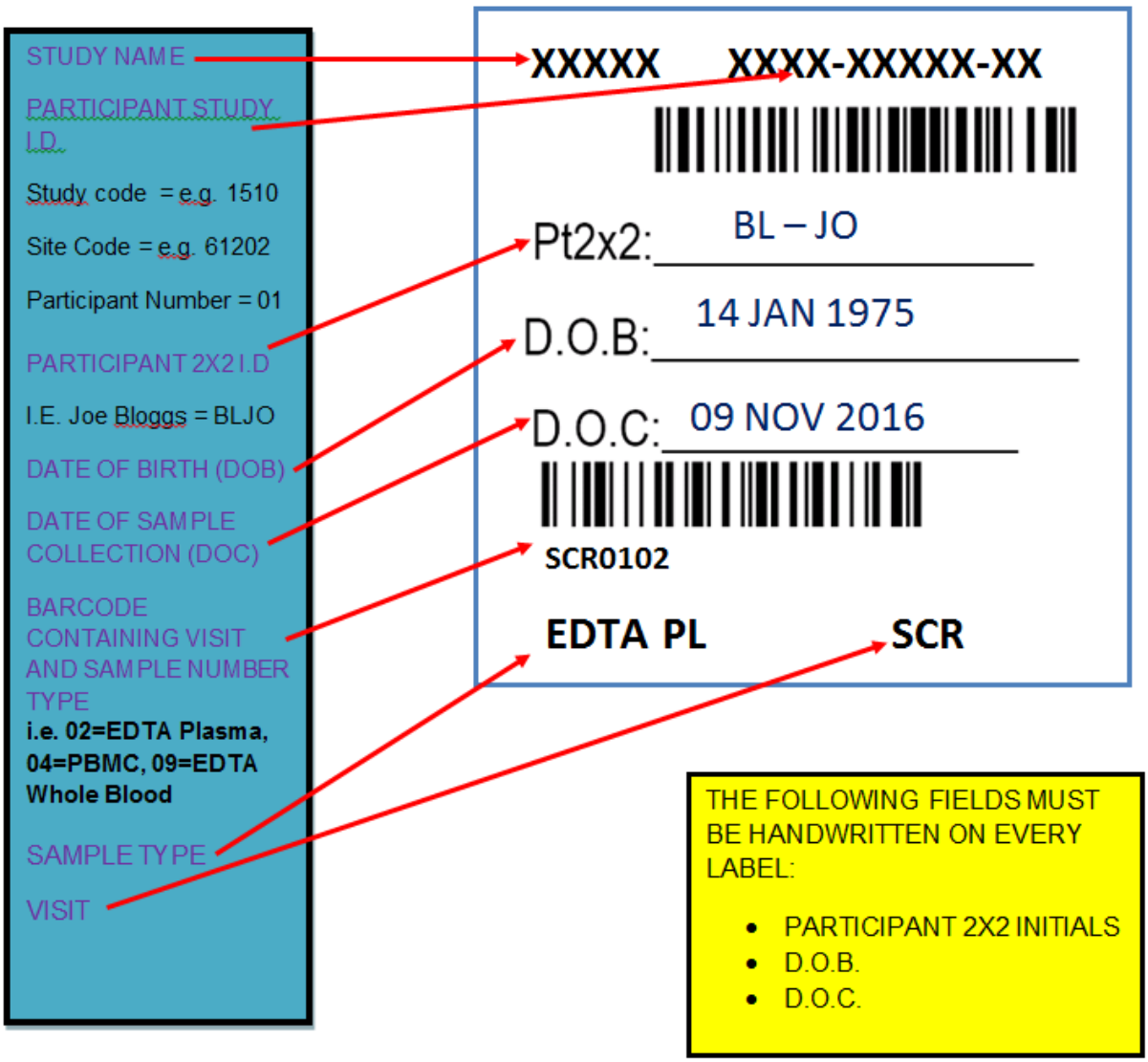


Figure 3: Understanding the aliquot labels

The following are some of the common visits and samples collected in VHCRP protocols. Refer to your ***study specific supplement*** for the visit sand sample required for each study.

Table 2: Understanding the aliquot labels

Visit Name	**Visit Abbreviation**
Screening	SCR
Baseline	BSL
Weeks 1 to 8	WK1 to WK8
End of Treatment	ETR or EOT
Sustained Virological Response Week 12	SVR12
Follow-up 1 to X	FU1 to FUX
Termination	TERM
Reinfection Follow-up 1 to X	RFU1 to RFUX
Sample Type	**Sample type abbreviation**
EDTA Plasma	EDTA PL
EDTA Whole Blood	EDTA WB
ACD Plasma	ACD PL
PBMCs	PBMCs
Buffy Coat	BUFFY CT
Dried Blood Spot	DBS

The aliquot labels may or may not be completed by the Study Site Coordinator (refer to section 4: study kit labels in the ***study specific supplement*** for further information). Tubes, aliquots and labels may be colour coded to make labelling easier as detailed in Figure 4. You must ensure the correct label goes on the correct aliquot so that we know what is in each aliquot, which participant the aliquot belongs to and which study visit the aliquot relates to.

EDTA plasma from the **LARGE PURPLE** tube (10mL EDTA) goes into the **PURPLE ALIQUOTS** and is labelled with the **PURPLE LABELS.**

Whole blood from the **SMALL PURPLE** tube (4mL EDTA) goes into the **RED ALIQUOT** (or brown aliquot tube for REACT) and is labelled with the **GREEN LABELS**.

PBMCs from the **YELLOW** tubes (9mL ACD) go into the **YELLOW ALIQUOTS** and are labelled with the **BLACK LABELS** (9mL ACD tubes are only used in some studies).

ACD plasma from the **YELLOW** tubes goes into the **BROWN ALIQUOTS** and are labelled with the **BROWN LABELS**

Buffy coat from the **LARGE PURPLE** tube (10mL EDTA) goes into the **2mL Sarstedt vials** and are labelled with **BLACK LABELS**

If coloured vials or labels are not provided, ensure that sample type on the vial label matches the contents of the vial.

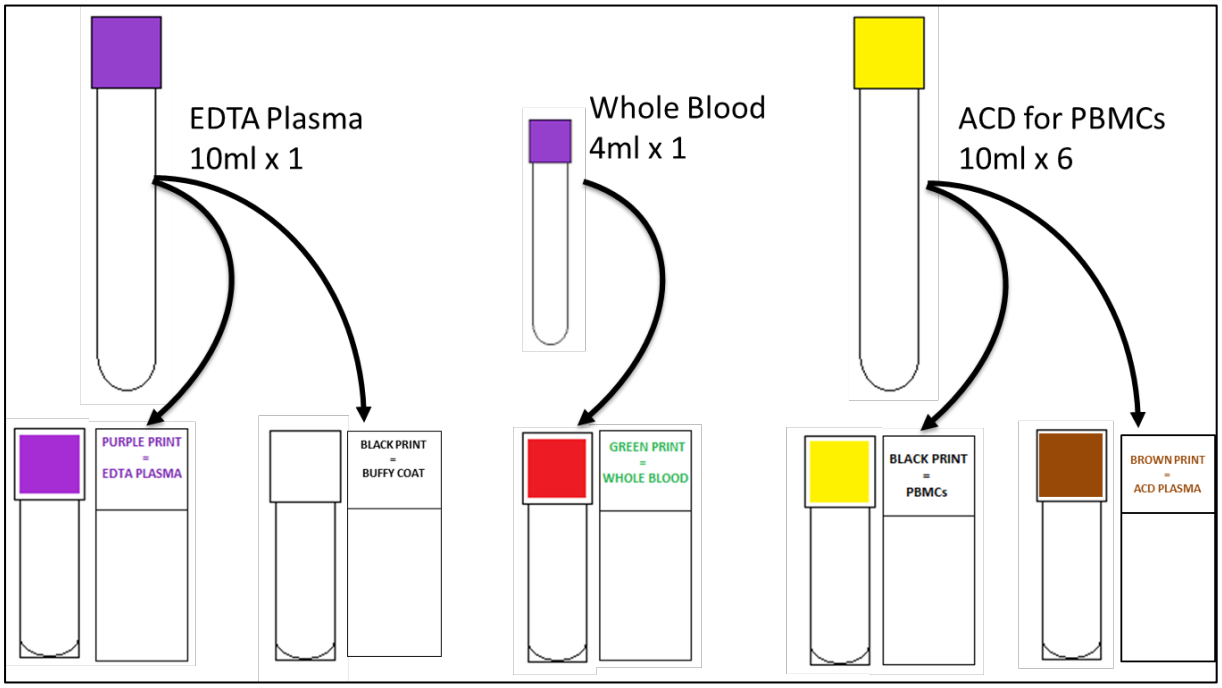


Figure 4: Specimen tubes, aliquot tubes and aliquot labels

7. Processing of Laboratory Samples for Study Visits

Detailed instructions are given below for processing of each sample type including flow charts outlining each step. It is essential that the processing instructions are followed exactly. This is because all samples from all sites must be processed in the same way to ensure consistency of results.

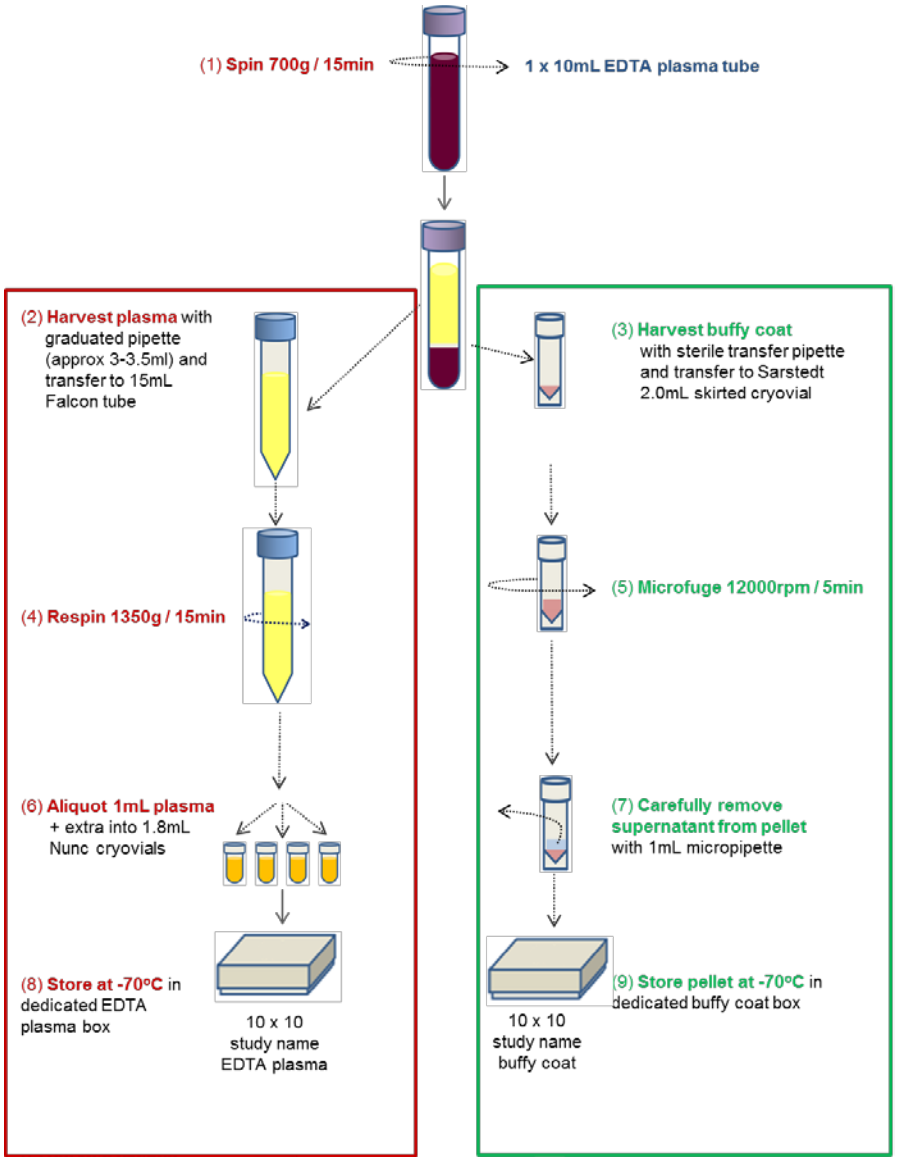
7.1 EDTA Plasma and Buffy Coat Preparation

(Note: Store whole blood at 2-25°C for no longer than 6 hours before processing from time of collection. If bloods received after 6 hours, still process but make this clear on request forms and in Labkey Offsite Repository).

A. For EDTA plasma:
   a. Centrifuge the 10ml EDTA tube of blood at 700g for 15min.
   b. Harvest the plasma and transfer it on a 15 mL falcon tube.
   c. Respin the harvested plasma at 1,350g for 15 min.
   d. Aliquot **1.0mL** of the plasma into 1.8 mL internal thread cryotubes, purple tops.

e. Log the sample details in LabKey Offsite Repository (see Appendix 1).
f. Store the aliquoted plasma at -80°C into designated EDTA plasma box (10 x 10 cryobox) labelled: **EDTA PLASMA** (Note: more than one box may be required.)

B. For Buffy Coat, if required
a. Following step 2 of above, Harvest buffy coat with sterile transfer pipette
b. Microfuge harvested buffy coat at 12000rpm for 5min
c. Carefully remove supernatant from pellet
d. Store the buffy coat at -80°C into designated buffy coat box (10 x 10 cryobox) labelled: **BUFFY COAT** (Note: more than one box may be required.)



7.2 ACD plasma/PBMCs Preparation

If ACD Plasma is being collected then an additional step in required as highlighted below. Otherwise continue processing without harvesting plasma.

(Note: Prepare cryopreservation media (FCS with 10% DMSO, fresh for 48hrs)).

NB. Before beginning, prepare cryoprotective medium fresh before each freezing procedure. Filter heat-inactivated FBS with 0.22µm syringe filter prior to use. Mix 90% filtered, heat-inactivated FBS to 10% DMSO. Date and initial storage container. Only make up requirements for 1 to 2 days at a time. Cool to 2-8°C prior to use.

Step 1 To facilitate the removal of plasma from clinical samples, centrifuge whole blood tubes at 200-400 xg for 15 minutes at 20-25°C.

Step 2 Harvest the plasma and aliquot 3 x 1mL ACD plasma into 1.8mL cryovials.

Step 3 Store the ACD plasma at -80°C into designated ACD plasma box (10 x 10 cryobox) labelled: **ACD PLASMA**

Step 4 Using a sterile pipette draw up the buffy coat layer from each of the collection tubes and pool in a 50mL falcon tube. Add a maximum of 15mL buffy layer per 50mL centrifuge tube – if you have more than this use two 50mL tubes. Add 1 to 1.3 parts of diluent usually RPMI-1640 (saline or PBS may be substituted) to the 50 mL centrifuge tube. eg. 15 mL centrifuged blood to 20 mL RPMI-1640.

Step 5 Underlay this mixture with 10 mL of Ficoll-Paque.

Step 6 Centrifuge at 400 x g for 20 minutes at 20-24°C (gradually increasing rpm to desired speed - brake off).

Steps 7-10 Carefully remove Ficoll-Paque / plasma interface containing lymphocytes and place into new 50 mL centrifuge tube. Add RPMI-1640 (saline or PBS may be substituted) to 45 mL and centrifuge at 400 x g for 15 minutes. Tip off the RPMI-1640 from the cell pellet after this first wash step (into a waste bottle) and resuspend the cells in 10mL RPMI-1640.

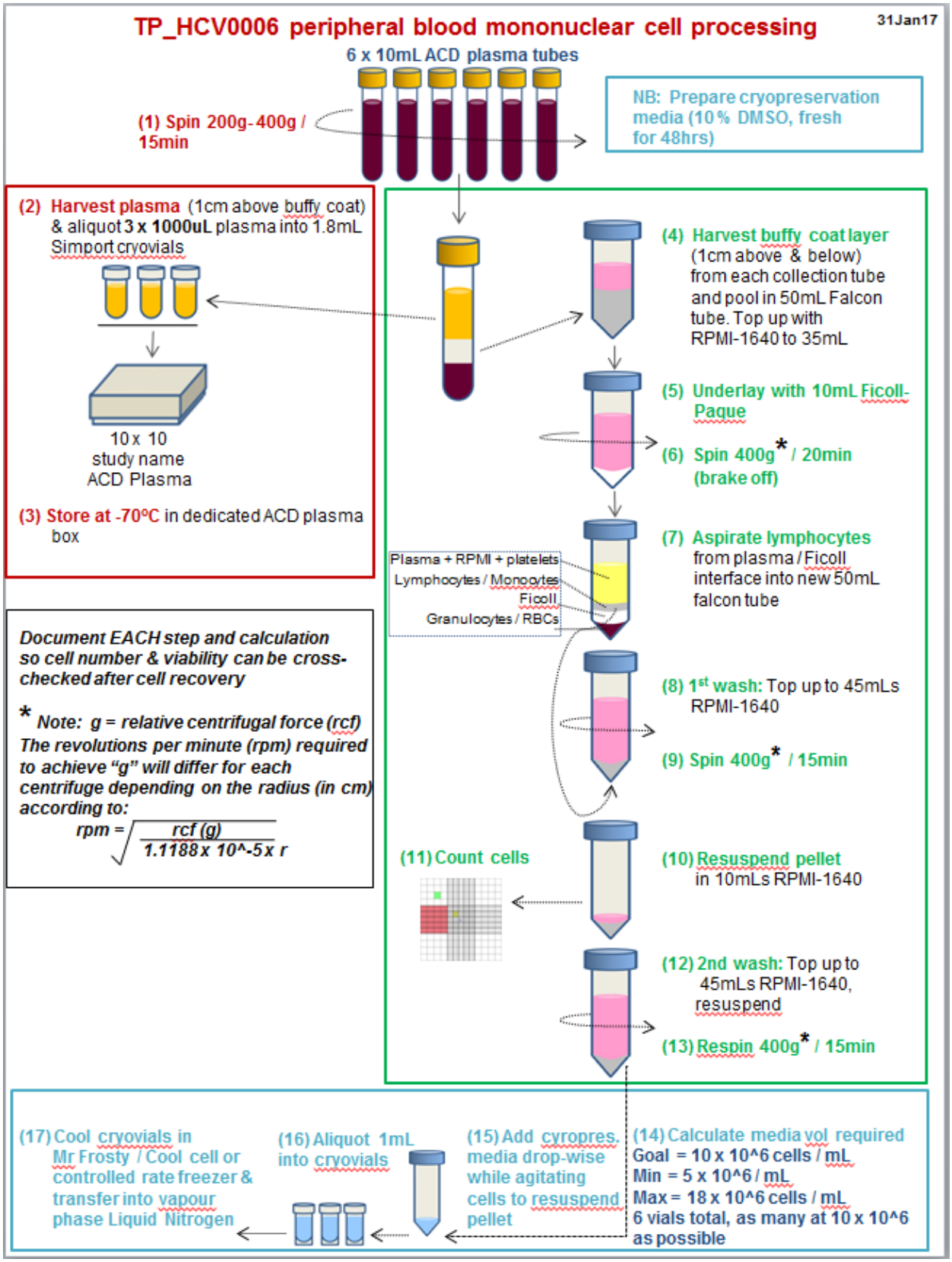
Step 11 Count cells, assess viability and calculate concentration of cells. Subject to the number of cells harvested (e.g. from 5 - 10 ml ACD blood tubes), perform an initial 1:5 or 1:10 dilution of the cell pellet in medium, followed by a 1:1 dilution in Trypan Blue (omit the initial dilution in medium if only 1 or 2 x 9ml collection tubes were processed). Load the haemocytometer with the Trypan/cell mixture to fill the area under the cover slip. Make sure the haemocytometer chamber depth is 0.1mm, and use the cover slip that is specific for the haemocytometer. Allow the cell suspension to settle in the haemocytometer for at least 30 seconds before counting. Count the 4 large corner quadrants (see diagram). Viable PBMCs will be clear; non-viable PBMCs will be blue. Do not count large cells of granulocyte appearance as being PBMC (these do not survive cryopreservation), so as to not overestimate the PBMC content. Include cells that touch either the top line or left vertical perimeter line of any corner square. Do NOT count any cells that touch either the bottom line or right vertical perimeter line of any corner square. record the total PBMC yield for each specimen according to the following formula:
(average counts/quadrant) ×104 × dilution factor (i.e. medium and Trypan dilutions) × sample volume (ml)

Steps 12-13 Top up centrifuge tube with RPMI-1640 to 45mL and centrifuge at 400 g for 15

minutes at 20-24°C. Remove supernatant.

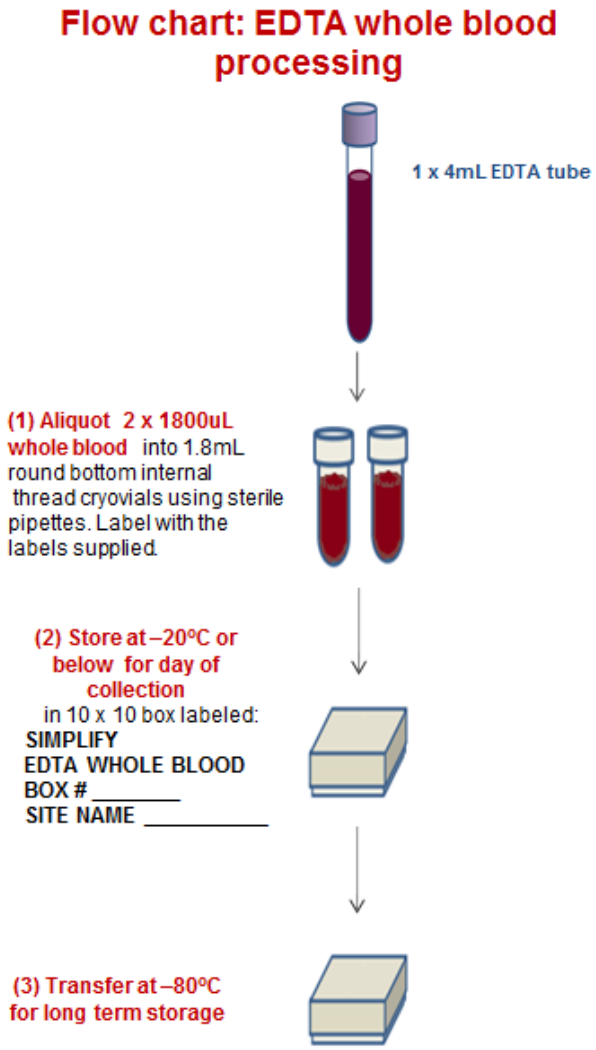
Steps 14-15 PBMC are resuspended to a concentration of up to 18 X 10^6 cells per millilitre with pre-cooled (~4°C) cryoprotective medium. The cryoprotective medium is added dropwise (to avoid hypotonic shock), on ice, with constant mixing, over 1 to 2 minutes.N.B: The concentration that PBMC ís are stored at varies according to requirement. A concentration of 10 X 10^6 / ml is generally considered ideal for later use in functional immunological assays.

Steps 16-17 Dispense 1mL aliquots of cell suspension into cryovials, on a bed of ice. Ensure that if the samples are to be frozen using a controlled rate freezer that the chamber is waiting at 4°C before adding the freeze media. At the end of the run the frozen cells should be transferred to a liquid nitrogen container in vapour-phase for storage. A NALGENE Mr Frosty may also be utilised. Place the cryovials into the Mr Frosty and then directly into a -70°C freezer for 12-24 hours (approximately 1°C drop per hour). The frozen cells should be transferred to a 10 x 10 cryobox labelled **PBMCs** in vapour-phase for storage at the next available opportunity. The position of the vial(s) should then be recorded in the appropriate inventory.


TP_HCV0006 peripheral blood mononuclear cell processing
31Jan17
6 x 10mL ACD plasma tubes
(1) Spin 200g-400g / 15min
NB: Prepare cryopreservation media (10% DMSO, fresh for 48hrs)
(2) Harvest plasma (1cm above buffy coat) & aliquot 3 x 1000uL plasma into 1.8mL Simport cryovials
10 x 10
study name
ACD Plasma
(3) Store at -70°C in dedicated ACD plasma box
(4) Harvest buffy coat layer (1cm above & below) from each collection tube and pool in 50mL Falcon tube. Top up with RPMI-1640 to 35mL
(5) Underlay with 10mL Ficoll-Paque
(6) Spin 400g* / 20min (brake off)
Plasma + RPMI + platelets
Lymphocytes / Monocytes
Ficoll
Granulocytes / RBCs
(7) Aspirate lymphocytes from plasma / Ficoll interface into new 50mL falcon tube
(8) 1st wash: Top up to 45mLs RPMI-1640
(9) Spin 400g* / 15min
(10) Resuspend pellet in 10mLs RPMI-1640
(11) Count cells
(12) 2nd wash: Top up to 45mLs RPMI-1640, resuspend
(13) Respin 400g* / 15min
Document EACH step and calculation so cell number & viability can be cross-checked after cell recovery
* Note: g = relative centrifugal force (rcf)
The revolutions per minute (rpm) required to achieve "g" will differ for each centrifuge depending on the radius (in cm) according to:
rpm = √(rcf (g) / 1.1188 x 10^-5 x r)
(14) Calculate media vol required
Goal = 10 x 10^6 cells / mL
Min = 5 x 10^6 / mL
Max = 18 x 10^6 cells / mL
6 vials total, as many at 10 x 10^6 as possible
(15) Add cyropres. media drop-wise while agitating cells to resuspend pellet
(16) Aliquot 1mL into cryovials
(17) Cool cryovials in Mr Frosty / Cool cell or controlled rate freezer & transfer into vapour phase Liquid Nitrogen

7.3 EDTA Whole Blood Preparation

A. Take out the lid of the 4mL EDTA blood collection tube.
B. Aliquot **1.0mL** of the whole blood sample into 1.8 mL internal thread cryovial tubes, red tops.
C. Log the sample details in LabKey Offsite Repository (see Appendix 1).
D. Store at -80°C or below in the 10 x 10 cryobox labelled: **EDTA WHOLE BLOOD**



7.4 DBS Preparation

C. The DBS card remains in the gas impermeable bag.
D. Log the sample details in LabKey Offsite Repository (see Appendix 1).
E. Store in the supplied freezer box at -80°C.

If extra supplies are required please contact the Study Project Coordinator

8. Completing the Laboratory Request Form

At all study visits the Site Study Coordinator will complete the *Laboratory Request Form* which is usually a three part (triplicate) non-carbon reproducing (NCR) form. The copies are different colours and should be kept as shown below.

- PINK copy to be kept by local laboratory;
- WHITE copy to be sent with samples to the Kirby Institute at the end of the study and upon Kirby Institute instructions;
- YELLOW copy remains with the Site Study Coordinator.
-

For most studies, the Laboratory Request Form is split into two parts.

a) For clinic use – this will be completed by the Site Coordinator

Details completed by the Site Coordinator are:

- Participant ID
- Participant Initials
- Date of Birth
- Collector's name
- Collection date
- Collection time
- Study visit
- Specimen comments

b) For processing site use only – this is to be completed by the processing laboratory

Details to be completed by the laboratory technician are:

- Specimen received date
- Specimen received time
- Specimen processed date
- Specimen processed time
- The number and type of samples stored
- Box number and positions of samples
- Confirmation of sample tracking in LabKey Offsite Repository
- Sample comments – details of any problems with the samples
- Name and signature of person who processed the samples

Please refer to the ***study specific supplement*** for study specific request forms.

9. Sample Storage

Please refer to the ***study specific supplement*** for the quantity and type of storage boxes that will be supplied to sites for the storage of samples.

PLEASE NOTE: Ensure you start with Box #1 when using the boxes provided for EDTA plasma, EDTA whole blood, PBMCs, ACD plasma, and buffy coat. These boxes are supplied pre-labelled with the Box Number.

Each 10x10 cryobox has 100 aliquot positions in it. Each position is numbered and it is these numbers which are used to indicate the location of each aliquot on the **laboratory** request form and in the sample tracker, LabKey Offsite Repository.

Care must be taken to ensure samples are placed in the box starting at position 1 and moving sequentially through to position 100. Do not leave empty spaces in the box. Store aliquots as they are received, do not group all samples for all visits for one participant together. See Figure 5 below which details how to store the samples.

1	2	3	4	5	6	7	8	9	10
11	12	13	14	15	16	17	18	19	20
21	22	23	24	25	26	Etc.			

Figure 5: Placing aliquots in the storage box in the correct order.

EDTA Plasma, EDTA whole blood, buffy coat, ACD Plasma and DBS samples must be stored at -80°C and PBMC samples must be stored at -200°C.

It is the responsibility of the site Principal Investigator or designee to ensure that the study central laboratory specimens are stored appropriately. Please refer to the ***study specific supplement*** for file note documentation to record where samples are stored and who is responsible for maintaining the samples.

Sample Storage conditions:

It is a requirement for clinical trials to document sample storage and to ensure that temperatures are maintained. The following are required:

- A daily temperature log for the freezer where the samples are stored must be maintained. Your local laboratory log may be used or alternatively the log provided in the ***study specific supplement.***

- The freezer must be alarmed and a procedure in place to ensure continued correct storage of the samples should the freezer fail.

- The Project Coordinator must be notified as soon as possible of any deviations above -60°C for samples that are stored at -80°C (EDTA plasma, EDTA whole blood, buffy coat, ACD Plasma and DBS), or a vapour phase tank failure for PBMC samples stored at-200°C.

Please refer to the ***study specific supplement*** for the sample storage temperature deviation form to notify the Project Coordinator of any temperatures deviations.

The laboratory sample storage and temperature logs will be checked during site monitoring visits.

10. Tracking samples in LabKey Offsite Repository

It is a requirement of clinical trials and ICH GCP that all samples collected are tracked and a log exists.

Studies will use **LabKey Offsite Repository** to track and log the research samples. LabKey Offsite Repository is a web based electronic sample tracking system that helps scientists organise, analyse, and share large quantities of biomedical research data.

You will be given a username and password to enter data into LabKey Offsite Repository which can be accessed by the Kirby Institute staff to review sample collection and storage. You will be able to add vials, mark vials as prepared for shipping or shipped. You will not be able to update visits, vial types, or box names.

Every sample from every participant and every visit must be tracked in LabKey Offsite Repository.

Details entered for each participant are:

- Participant ID (or screening ID)
- Date of Birth
- Visit name
- Specimen comments

Then for each aliquot (or DBS card, as required) the following are also entered:

- Sample type
- Volume (or cell count for PBMCs)
- Box number
- Position number (not applicable to DBS)
- Sample comments

There should be one row per aliquot/DBS card.

Complete step-by-step instructions on how to use LabKey Offsite Repository are located in **Appendix 1**.

11. Filing Laboratory Request Forms

It's a requirement of clinical trials to retain all source documents for the duration of the study and for at least 15 years or as per local requirements following the end of the study. This includes laboratory request forms. Therefore each laboratory request form must be filed.

There are plastic sleeves in the ***study specific supplement*** section for file note documentation to record where samples are stored and who is responsible for maintaining the samples and for filing the laboratory request forms. If coloured laboratory request forms are used, separate the pink and white copies and file both in the correct plastic sleeve.

- The pink copy will remain at the site
- The white copy will be shipped with the samples to the Kirby Institute.

12.Shipping Samples to the Kirby Institute

During or at the end of the study you will be asked to ship the samples to the Kirby Institute. The study Project Coordinator will contact you and arrange a courier and provide all shipping instructions.

The timing and frequency of sample shipment will depend on the study. Refer to the ***study specific supplement*** for details.

Do not ship the samples until you have been requested to by the study Project Coordinator.

13.Quality Assurance

The Kirby Institute Monitor may conduct periodic quality assurance inspections throughout the study. The monitor may review the following items:

- Temperature logs;
- Laboratory Request Forms;
- Laboratory manual;
- Samples;
- LabKey Offsite Repository.

The study monitor will notify the laboratory at least two weeks prior to any inspection and will provide a list of items required to be available on the day/s of the visit for inspection. Following the inspection a report will be provided to the Study Principal Investigator documenting the inspection and summarising any findings or action items to be followed up by the laboratory.

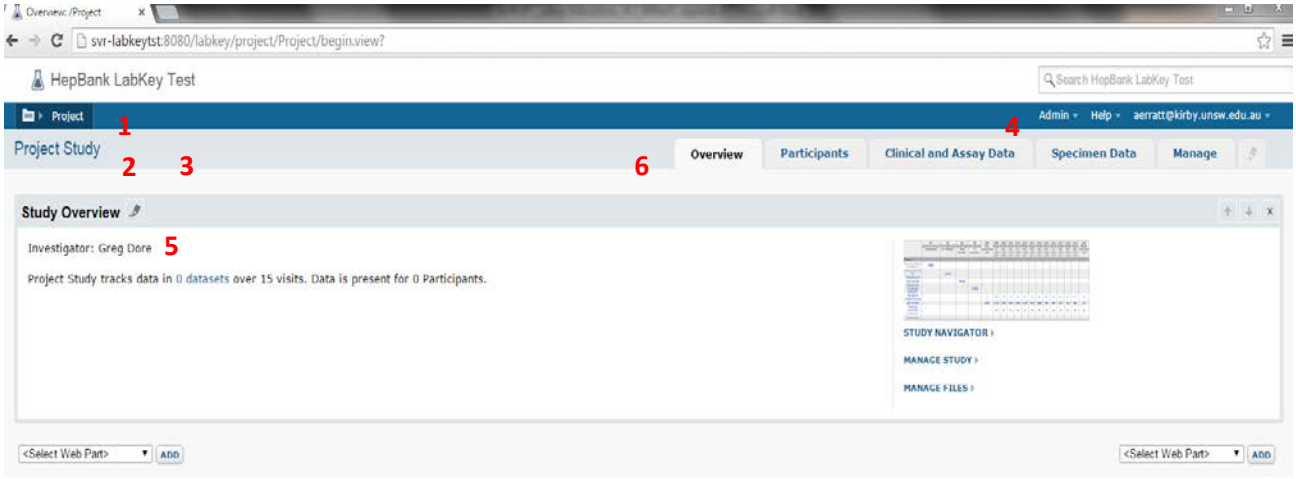
14.Trouble Shooting

Study contacts are to be found in the ***study specific supplement***. They are available to answer any questions or assist in the event of problems.

Appendix 1 – LabKey Offsite Repository user manual

Below is an overview of **LabKey Offsite Repository** and an explanation for access to your Offsite Repository.

Overview Image



1. **Site Name:** in this case it is called Hepbank. This is also a hyperlink, which when clicking will take you back to the home project for the site.
2. **Project Folders:** This will list the currently active folder (in bold) and any sub-folders that may exist.
3. **Projects:** This will list all existing projects for your site that you have access to.
4. **Global Set of Menus:** If you are an Administrator for the site or the currently active project, there will be an admin menu where you will be able to manage the project or site. A help menu which links to the support project folder and the official Labkey Offsite Repository documentation (external). Finally, your username/display name, where you will be able to update your account information (e.g. display name, phone number, password) by clicking on the My Account link, or sign out.
5. **Title of the Current Project Folder:** Most of the time, this will be exactly the same as the project folder (point 2), but in some circumstances, it will be different such as in a study. This is also a hyperlink, which when clicking will take you back to the home of the project folder you are currently in. It has the same effect as if you clicked on the bold project folder from section 2.
6. **Some projects** such as a study will be conveniently organised into separate tabs. Here you can easily navigate between the different sections.

1. Returning to the Main Project Folder

When you are in a project, you may need to return to the main page of that project. The easiest way to achieve this is by clicking on the project name or project title links respectively (Please refer to section 2 and 5 of the overview image, respectively).

2. Accessing your study

To access the LabKey Offsite Repository, please enter the following URL:

https://labkey.kirby.unsw.edu.au/labkey/project/home/begin.view

You will then be asked to enter your email address and selected password. Once the page is loaded, click on the Offsite Repository beneath the Project List on the left hand side. From there, you will proceed to submitting vial information for the study.

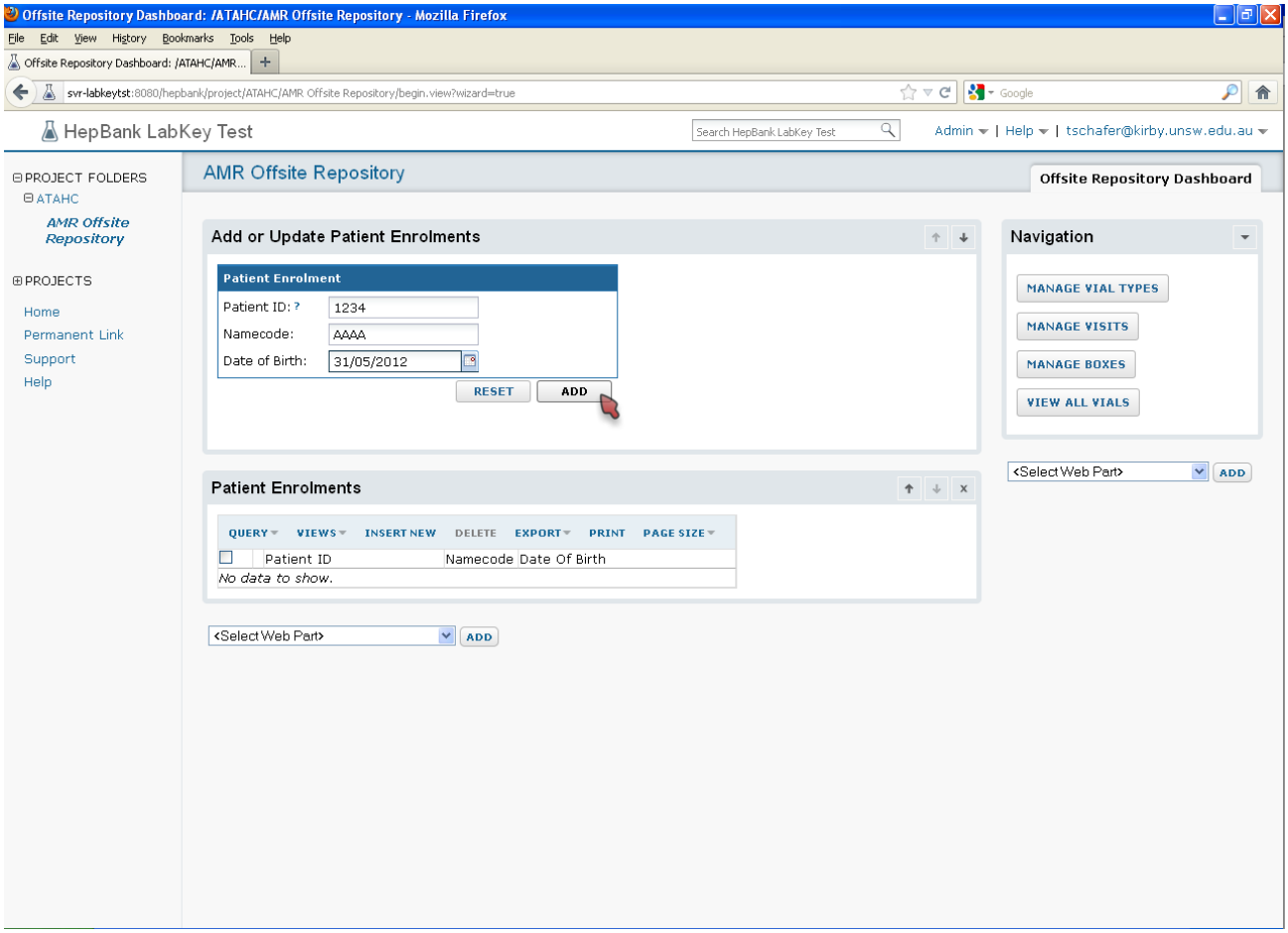
3. Adding/Editing Participant Vials

This is divided into a number of steps: participant enrolment → participant visit → participant vial. The first step is to add the enrolment, after clicking save, the page is reloaded, and the visit form becomes visible. Once the visit is saved, the page is reloaded and the vial form becomes visible.

Step 1. Add/Edit a Participant Enrolment

From the main page of the project, complete the details of the participant screening visit and click **ADD**. For studies where a Screening ID is assigned, the Screening ID should be used for the screening visit only. At baseline the participant will need to be enrolled into LabKey Offsite Repository a second time using the Participant ID instead of the Screening ID. Enter the screening ID in the visit comments at the baseline visit.

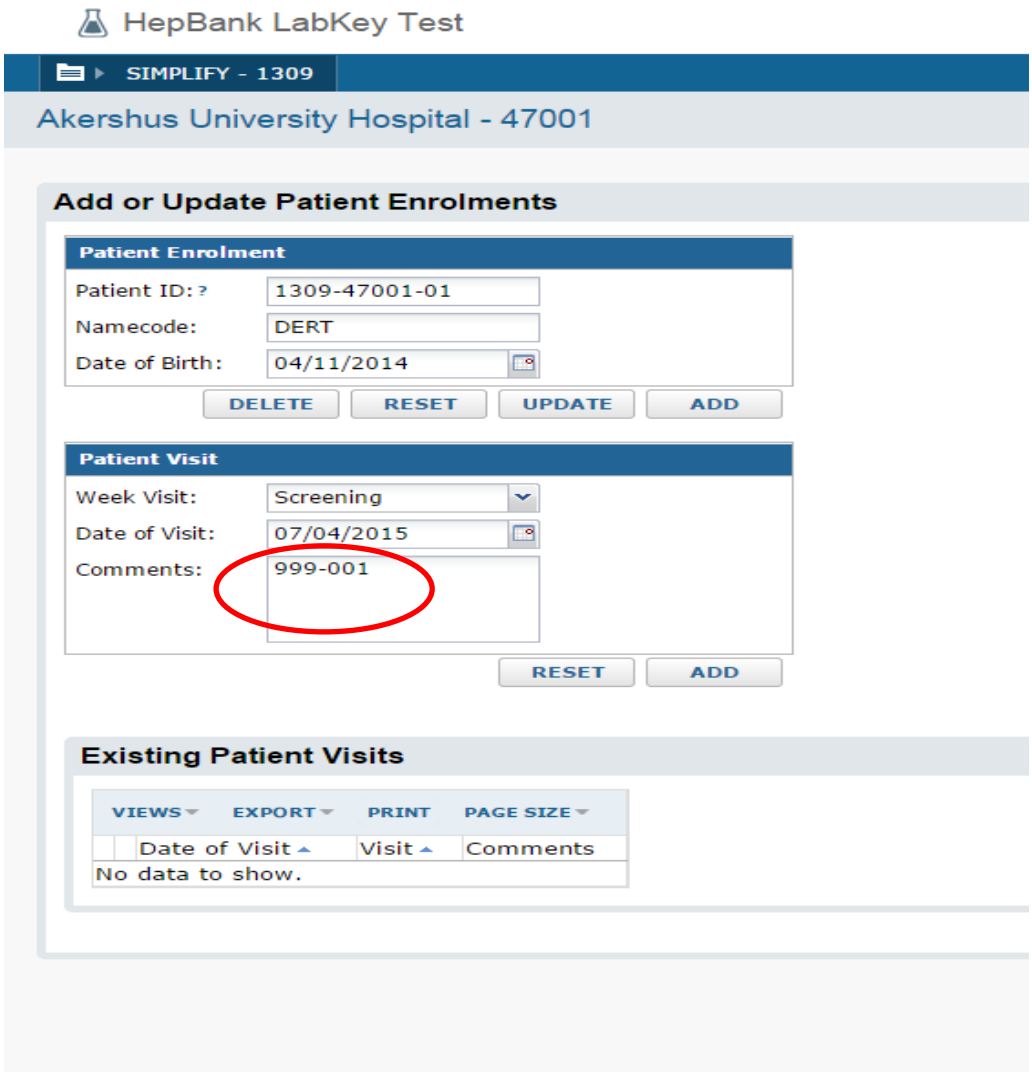
Note: For studies where a Screening ID is assigned, each participant will need a second enrolment using the Participant ID once the participant completes the baseline visit. Do not enter treatment visits under the screen participant number.



Alternatively, if you wish to edit a different participant enrolment, go back to the projects main page by clicking the Offsite Repository name in the left hand column. Down the bottom is a data grid of existing participant enrolments. Simply click **EDIT** on the participant you either want to edit vials entered previously, or to addanother visit.

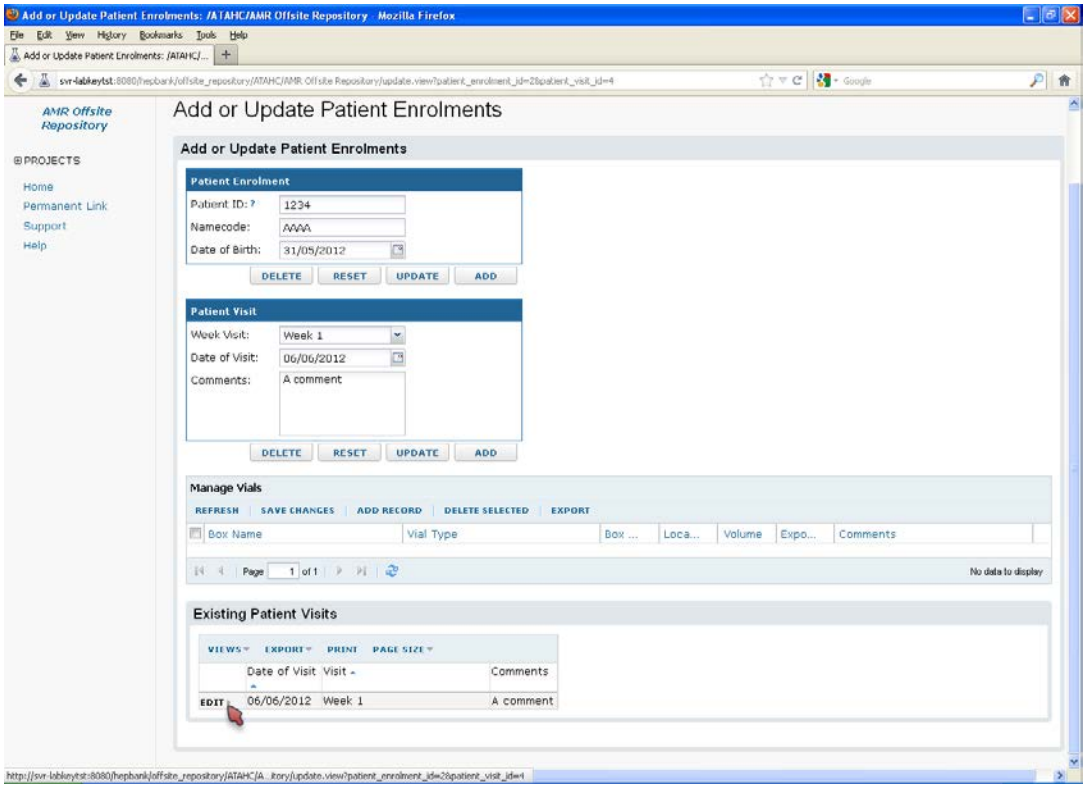
Step 2. Add/Update a Participant Visit

Complete the details for the participant visit – with a date of visit on or before the current date (which will then associate with the participant ID who you are currently editing) and click **ADD**.



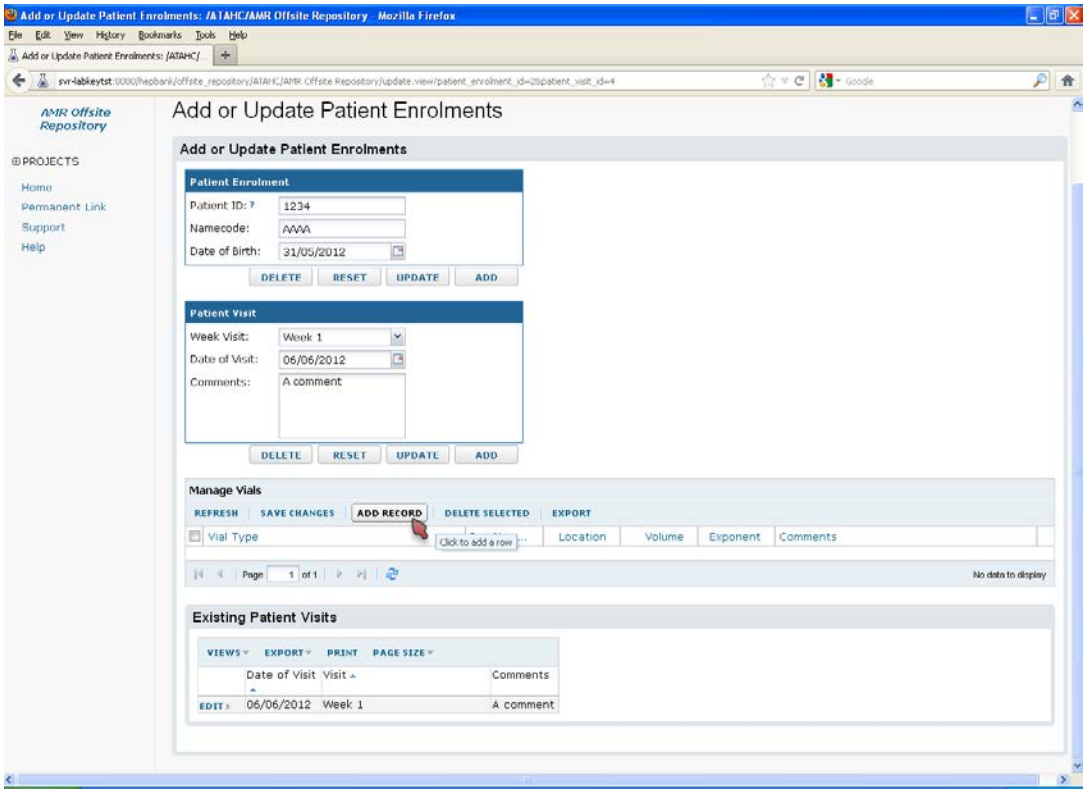
Please note: At Baseline, please remember to record the SCR ID in the comment box of the Participant Visit (see above).

On this page, the list of visits associated to the participant enrolment is displayed at the bottom of the page. If you wish to edit vials for an existing visit, scroll down to the bottom of the page. There will be a data grid of existing participant visits against the participant. Simply click **EDIT** on the one you want to add a vial to.

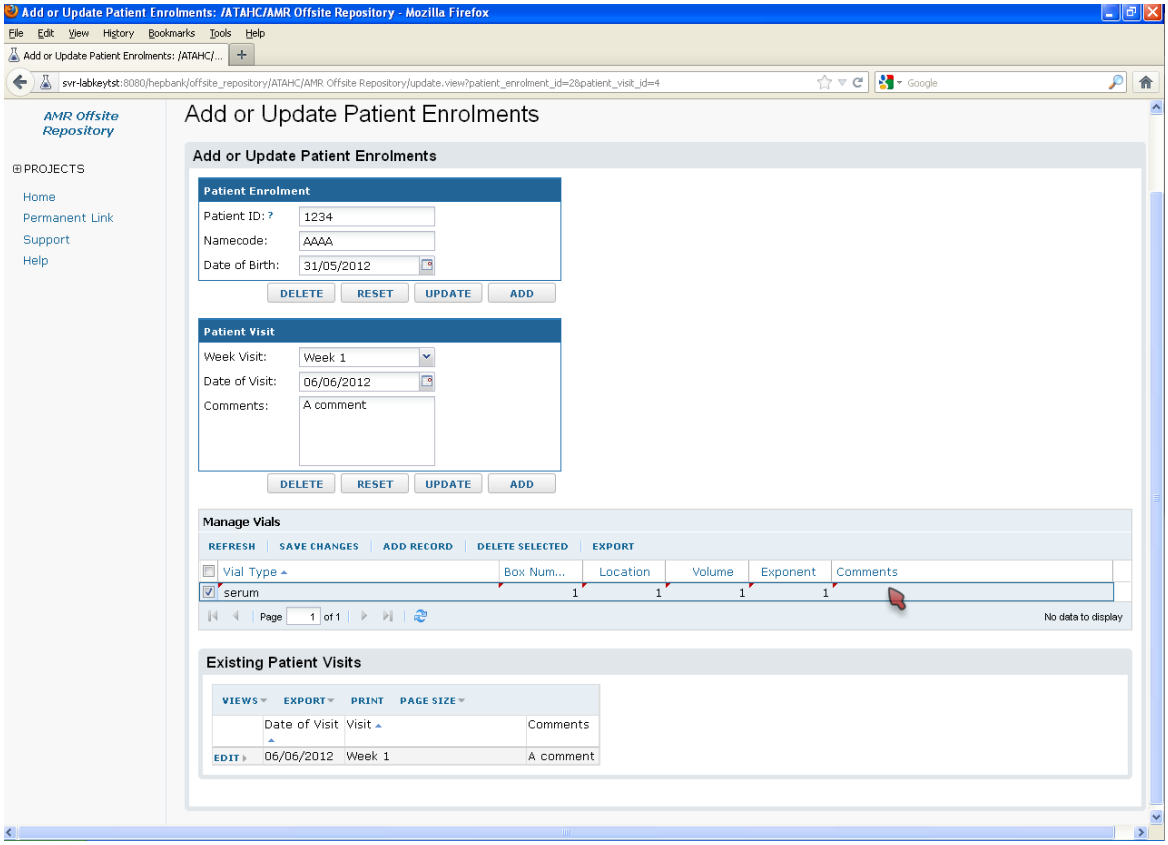


Step 3. Add/Edit a Participant Vial

Below the participant visit form, there is a Manage Vials data grid that you can add rows to and easily update existing records. To add a new row, click on the **ADD RECORD** button.



To move between fields you can either **TAB** or **DOUBLE-CLICK** on the field. Complete the fields – at a minimum, you need to have **VIAL TYPE** (a specimen type drop down list is provided), **BOX NUMBER** (the box the tubes are to be stored in has the Box Number written on it e.g. Box Number: 1309-L61202-02-**01**←these last 2 digits are what is required to be recorded for LabKey Offsite Repository), **LOCATION** (i.e. the grid position number of the vial within the box) and **VOLUME** (i.e. the volume or cell number factor of the specimen). Not for a PBMC cell count, the fraction component of the concentration is entered into Volume, and the exponent value stored in **EXPONENT** (e.g. For a cell count of 7.5e^6 it would be entered as volume=7.5 and exponent=6). You will see each field with a modified value will have a red icon in the upper left area of fields' box.



To save any changes, click the **SAVE CHANGES** button. It is worth noting that if one of the required fields has no value, clicking the **SAVE CHANGES** button will have no effect. When the red icons disappear, it means the record has been saved.

Step 4. Deleting Participant Vials

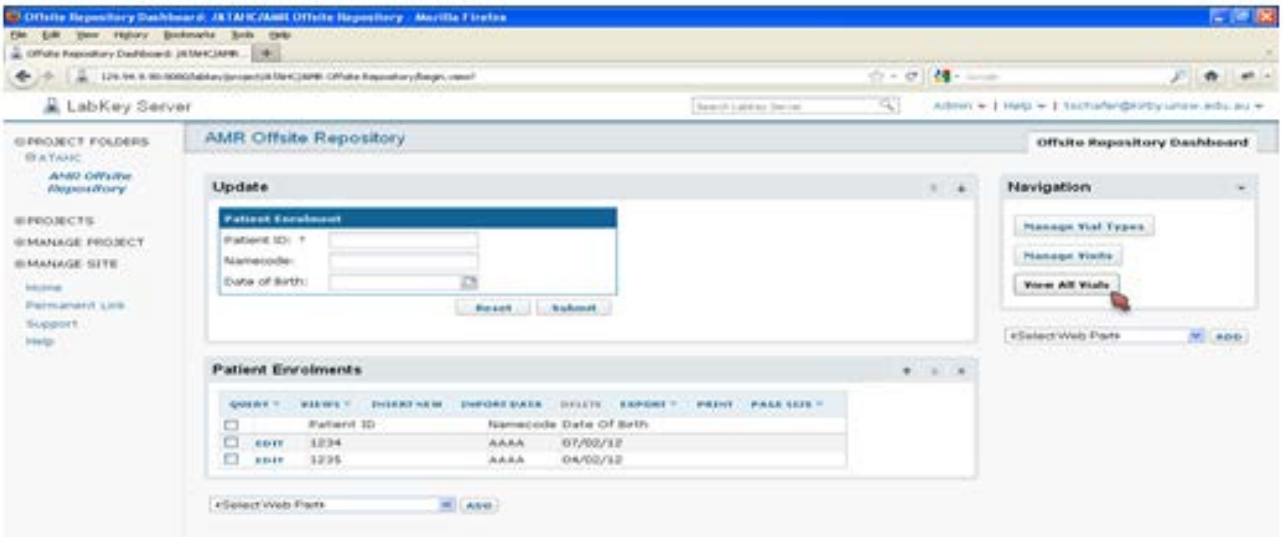
You will not have permission to delete participant enrolments and participant visits but you will be able to **DELETE VIALS**. To delete a participant vial, place a tick in the vial you wish to delete, and click the **DELETE** button at the top of the grid view. Confirm you wish to delete the vials by clicking **DELETE** again.

4. Vial Workflow

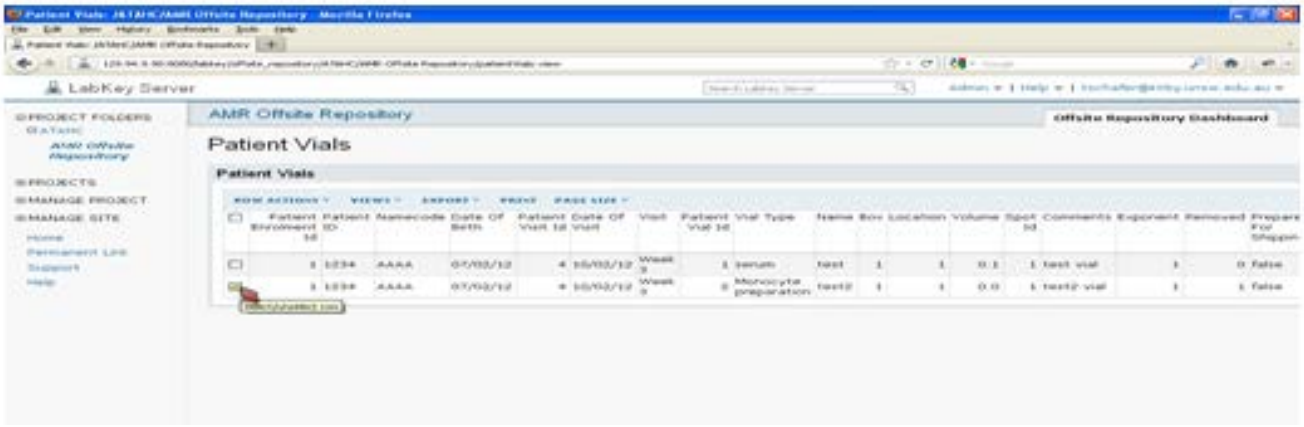
The work flow is split up into 4 statuses for processing vials:

1. Prepared for Shipping
2. Shipped
3. Received
4. QC checked

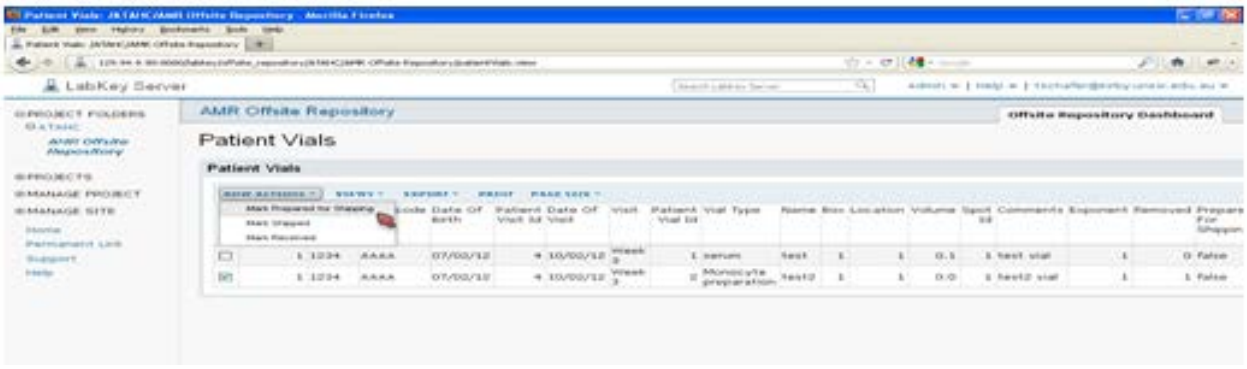
<u>Please note:</u> Each vial can only be given each status once. The first two are designed to be applied by the local laboratory i.e. Mark Prepared for Shipping, Mark Shipped. The third will be applied by a Kirby Institute staff member i.e. Mark Received, QC Checked. To apply a status to a vial, or series of vials, return to the main project page, click on **Offsite Repository Dashboard** in the top right hand corner, then on **VIEW ALL VIALS** in the **Navigation** box below.



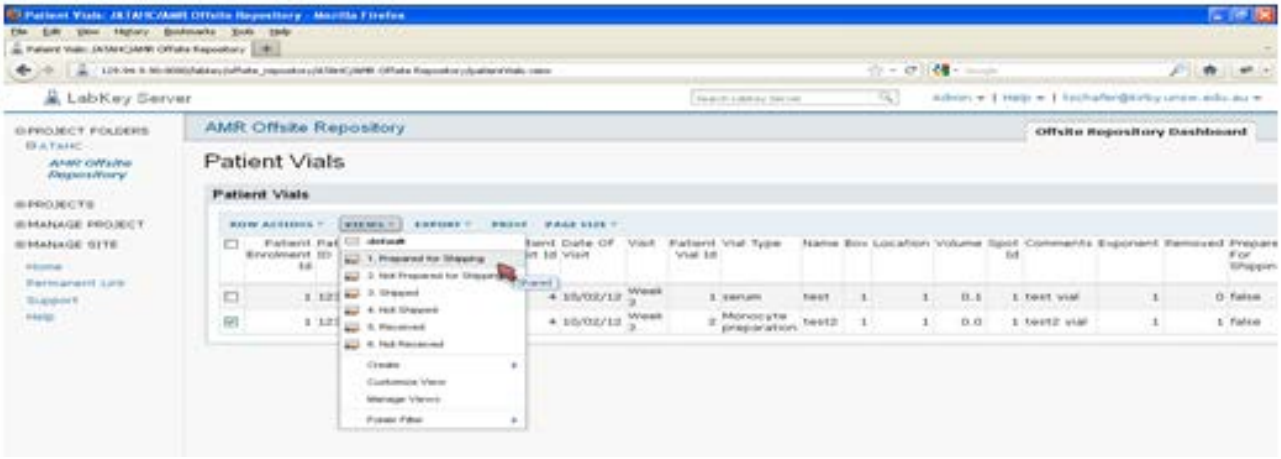
It may be necessary to filter the rows accordingly – once you have found the vials you want to apply a status to, place a tick in the checkbox against the row.



At the top of the data grid, click the **ROW ACTIONS** Button and select the relevant status.



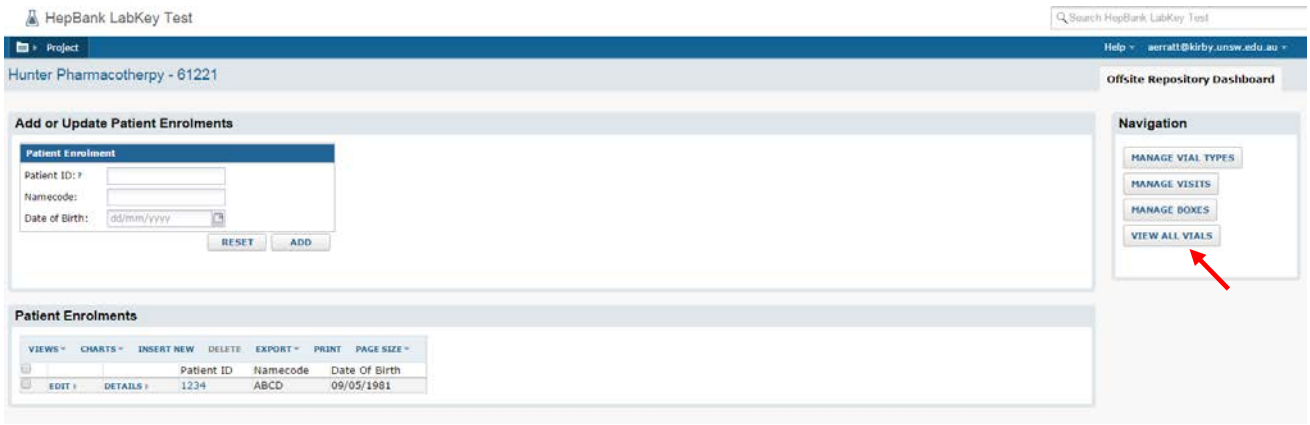
You can easily filter the vials by selecting one of the pre-defined views. Click the **VIEWS** button and select the view for which you want to filter the rows by.



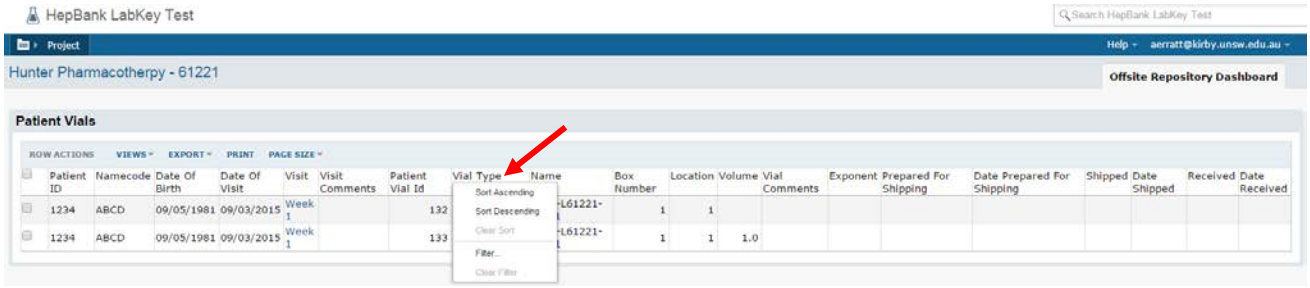
5. Selecting Samples For Shipment and Marking as Shipped

Study samples may be shipped during or at the end of the study, when bulk research samples need to be shipped to the Kirby Institute. In order to mark samples as shipped:

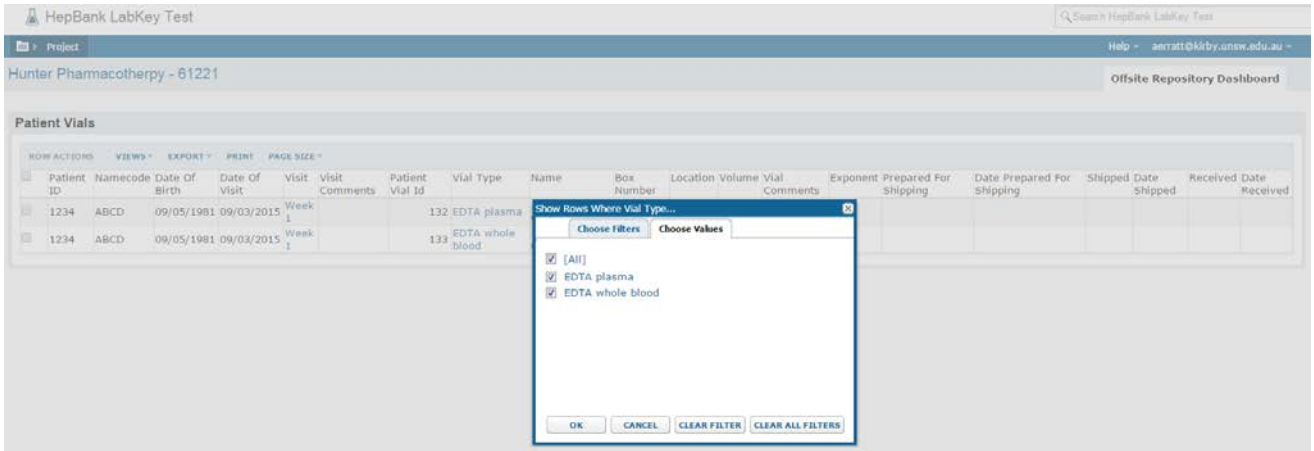
i. From the main repository screen select “View All Vials” as indicated by the arrow.



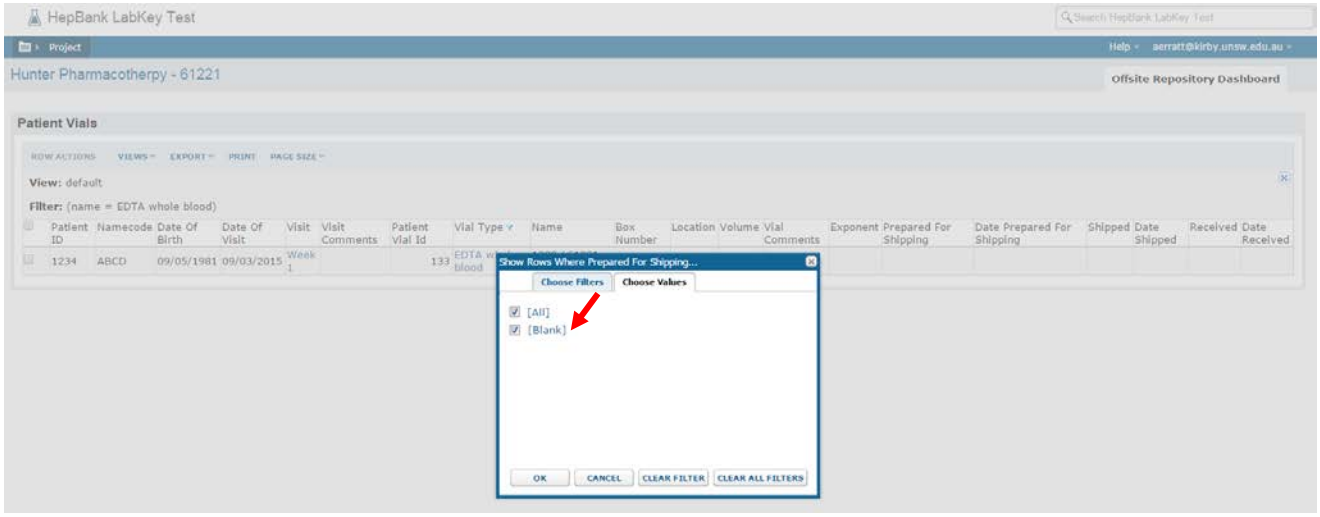
ii. Click on the Vial Type Box and select "Filter" from the dropdown box as indicated by the arrow.



iii. A box will appear "Show Rows Where Vial Type...". There are two tabs at the top – click on the "Choose Values tab". Using the mouse deselect all tick boxes apart from those samples to be shipped e.g. EDTA whole blood and click OK.



iv. All vials that have been entered into Labkey Offsite Repository for this vial type will appear. In order to only view vials that are in the laboratory and have not been shipped already go to the "Prepared for Shipping tab", right click to filter and select "Blank" as shown.

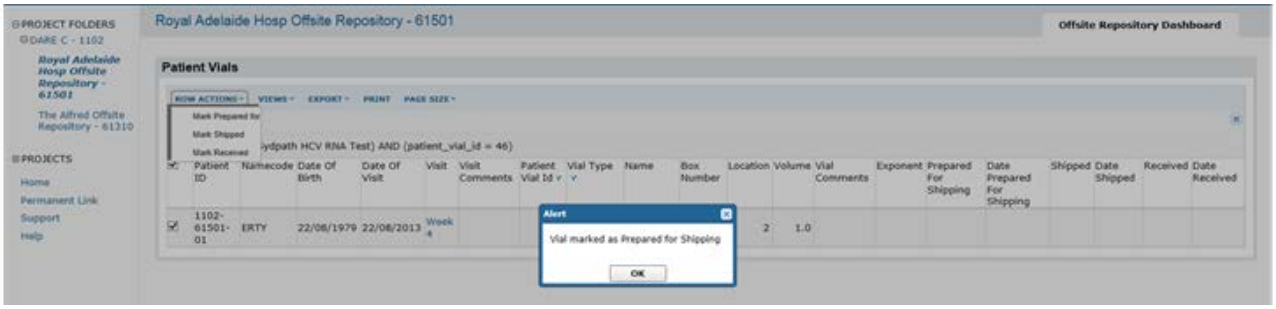


v. This will display only vials for the particular vial type to be shipped as per below. Mark the tick box on the left for aliquots to be shipped (this should be all vials displayed).

vi. Go to the "Row Actions: tab (underneath Participant Vials) and from the dropdown box select "Mark Prepared for Shipping". Once selected and OK is pressed, "True" will appear in the "Prepared for Shipping" column and today's date will appear in the "Date Prepared for Shipping" column as shown by the purple arrow.

Note each sample in Labkey Offsite Repository can only be marked as prepared for shipping, shipped or received once. If extra samples need to be marked as prepared for shipping or shipped, samples that have already been allocated this status must be un-ticked before extra aliquots are marked/ticked then assigned the same status, otherwise an error message will appear.

vii. A confirmation message will appear:



viii. Proceed to book courier and dispatch samples as per instructions provided by the Project Coordinator. Once samples have been collected log back into LabKey Offsite Repository, repeat the above steps i) to iii). Note vials marked as prepared for shipping will have a "True" status in the "Prepared for Shipping" row as indicated but the "Shipped" and "Date Shipped" columns will be empty.

Click on the "Prepared for Shipping" tab, select "Filter" and select "True", then click on the "Shipped" tab, select "Filter" and select "False". This will display all vials prepared for shipping but not actually shipped. Mark all vials using the tick box on the left then go to "Row Actions" tab and select "Mark Shipped" from the drop down box. Cross check the sample ID's selected against the sample shipment list before marking samples as Shipped.

ix. Today's date will then appear in the "Date Shipped" column as shown.

6. Data change procedure:

During the course of a study it may be necessary to change data entered into the research laboratory databases.

Types of errors can be:

- Participant ID errors including hyphen not used in participant ID or wrong ID entered
- Data entered into wrong participant
- Wrong details e.g. incorrect DOB entered for participant
- Visit/event error including wrong visit/event been assigned.

If any error is identified, the Project Team should be informed and will propose action:

- A Research Laboratory Data Change Form should be completed and sent to site.
- Site authorise proposed action by signing the Data Change Form.
- HepBank Laboratory personnel agree to the proposed action by signing the Data Change Form and make changes in the database (s).
- The Completed Research Laboratory Database Data Change Form filed in the Trial Master File.