

kConFab Procedures Manual

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Laboratory Protocols:

Biospecimen protocol

The following protocol is currently used by kConFab, it is based on the protocol used by the NIH for biospecimen collection

The minimum blood biospecimen collection would be X6 500ul plasma, BP for DNA, red cell fraction for RNA, WBCs maybe optional.

QA on DNA and RNA to be carried out as recommended by the NIH on randomly chosen samples every month (10%). The QA method currently used is as follows:

QA of whole blood

- (a) DNA is made from 1/4 of Guthrie card spot and 1/4 of the BP from the same participant using Qiagen whole blood DNA kits (cat # 29106).
- (b) A PCR using 5 different microsatellite markers is performed and then run on a sequencing gel
- (c) The DNA profile of Guthrie card vs BP is assessed for each participant.
- (d) If either the Guthrie card or BP DNA doesn't amplify for any one sample, the DNA extraction is repeated, PCR amplified and re analysed.
- (e) All errors between guthrie card vs BP DNA will be immediately reported. DNA re extracted and re analysed.
- (f) Should discordance between the guthrie card vs BP still occur, the laboratory manager will report to the chairperson of the biospecimen committee, one correction option would be to recommend that the sample be disposed of and the participant re bleed is possible.

QA of EBV cell lines:

- (a) As determined by the biospecimen committee, EBV cell lines are made from selected participants using one of the WBC/DMSO freezes. (page 14-17)
- (b) DNA is made from 1/4 of guthrie card spot and 1/4 of the EBV cell pellet from the same participant using Qiagen whole blood DNA kits.
- (c) PCR and gel analysis is performed and assessed as for the whole blood DNA QA protocol.
- (d) Discordance between the guthrie card vs EBV cell pellet DNA will be reported and acted upon accordingly.

A. Blood collection

We plan to collect 2 tubes (18-20mls) blood and so this protocol is for this amount (or less, as will sometimes come). We are collecting both of these tubes in EDTA tubes (ACD tubes to be used for New Zealand blood collections).

The protocol aliquot's 20mls blood into:

	Storage
1. 2 cards of Guthrie spots (from <1ml) for direct PCR	at RT
2. 6 freezes of plasma	in -70
3. 3 freezes of white blood cells (WBC) for transformation (from 9-10mls blood)	in LN
4. 1 freeze of non-lymphocytes (NL, from same 9-10mls) for RNA	in -70
5. 1 blood pellet (BP) from 9-10mls, for DNA isolation	in -70

B. Processing of blood:

- *TREAT ALL BLOOD AS POTENTIALLY INFECTIOUS.*
- *PROCESS IN A LAMINAR FLOW HOOD AND WEAR GLOVES AND GOWN.*
- *CHECK YOUR HEP B TITRE EVERY 2 YEARS.*
- *ENSURE THAT ALL STAFF WORKING WITH HUMAN BLOOD ARE FAMILIAR WITH THE PMCI LABORATORY SAFETY MANUAL ISSUED BY THE PMCI RESEARCH SAFETY OFFICER.*

All plastic wear etc needs to be sterile as these cells may one day be cultured; use standard sterile techniques.

Process blood within 24-48 hrs of being taken. Keep blood at room temperature until processed.

Receipt of blood

Label all tubes and Guthrie cards with name, DOB and appropriate kConFab numbers. The code pattern used for unique kConFab numbers is as follows:
UPN - Unique Personal Number = XX.XXX.XXXX
UFN - Unique Family Number = XXXX.XX.XXX
The PMCI biospecimen number is the last 2 digits of the year followed by the next consecutive number
eg 99/1000

Making guthrie spots:

- a) Mix blood thoroughly by inversion before starting. Wipe top of vacutainers with EtOH before opening.
- b) use the fullest vacutainer to make two full Guthrie cards by placing a drop of blood in the circles.
- c) Air dry thoroughly (a few days). Maybe dried with hair dryer or heat lamp.
- d) Store in paper envelopes in plastic containers away from rats!!.

ALWAYS make Guthrie cards, regardless of volume received

IF 20mls BLOOD RECEIVED:

use one tube for Ficoll isolation of WBCs and NL freeze, and one for Guthrie and BP for DNA. One Guthrie card is to be sent to the Westmead Hospital as a back up of biospecimen material. Please refer to **Back up of biospecimens**, page 11).

3) Spin for plasma:

- a) spin one vacutainer (about 9mls) at 1300-1500 rpm for 10-15mins to separate plasma
- b) remove 0.5 mls (500ul) into each 6 labelled freezer tubes
- c) store the 6 aliquots at -70

4) Separate WBCs by Ficoll gradient:

- a) transfer the remaining blood from this plasma spin to a labelled 50mls tube that has had 10mls RPMI placed in it
- b) aliquot 3 mls Ficoll into 2 labelled 10mls centrifuge tubes
- c) carefully layer the blood onto the Ficoll.
treat gently, don't mix, spin asap

d) spin at 1600 rpm in centrifuge for 30 mins, WITHOUT A BRAKE

e) collect the WBCs (second layer) with a sterile pipette and place into a 50ml tubes that has 25 mls RPMI. Use a swirling motion to "vacuum up " the WBCs. Don't take to much Ficoll (third layer) from below the cells as it is toxic to the cells.

** continue to process red non-lymphocyte (NL) fraction as below in italics

f) spin at 1600 rpm for 10 mins.. Brake can be used here.

** combine red NL fraction in one 10mls tube that contains 5mls RPMI and spin them with WBCs, ie 1600rpm for 10mins.

g) pour off the supernatant from the WBCs carefully into a waste container. resuspend the cells by flicking the bottom of the tube, add 3 mls of freezing mix to cells

**collect 1 ml of red NL and add to 400ul of freezing mix in freezing vials

h) dispense WBCs into 3x2mls freezing vials (all freezing vials with appropriate name and number). Place WBCs and NL on ice for a few minutes, no more than 10mins.

i) place NL in -70, DMSO is toxic at RT

j) Place the x3 WBCs into the -70 using two different storage containers, 2WBCs vials into one storage container, 1 WBC vial into the other
Transfer to LN downstairs within the month, again into 2 different storage vats.
The boxes with the 1 WBC vial are to be transferred as back up stock to the Epidemiology/Genetic Department, The University of Melbourne on a regular basis. Please refer to **Back up of biospecimens**, page 11).

5) Lyse red blood cells to make blood pellet (BP) for DNA isolation:

a) transfer blood from remaining vacutainer (usually tube to make the Guthrie cards) to a labelled 50mls tube.

b) fill tube with x1 TE. Mix vigorously. Place on ice for 2-5mins.

c) Spin at 2500rpm for 10-15 mins, this may make the pellet firmer (the pellet can be slippery!)

d) carefully pour off the supernatant into a container and add another 50mls of x1 TE solution to the pellet. Shake vigorously. Place on ice for 2-10mins.

e) spin for 10-15mins at 2500. Repeat washing if red cells persist..

f) carefully pour off supernatant and transfer "BP" with a small volume of supernatant to a labelled BP freezing vial. Store at -70 until DNA is required/isolated.

If 11-19mls of Blood is received:

- * make 2 Guthrie cards
- * use 9mls for plasma and 3 WBCs plus 1 NL freeze as above
- * use remainder for BP (can rinse the tube out if not a great volume)

The only change here is that there is less blood is used for the PB

If 6-10mls blood is received:

- * make Guthrie spots
- * use rest for plasma, 3 WBCs plus 1 NL freeze
ie make 2-6 plasma aliquot's
place the remaining blood into RPMI and do Ficoll gradient, 2-3 freezing vials
- * wash tube out with EDTA to get BP, although, this may not be possible

If less than 6 mls blood received:

- * make 2 Guthrie cards
- * use rest for plasma, place remaining blood in RPMI and collect 1-2 WBCs and NL

ie, no BP is made, fewer plasma freezes and only 1-2 WBCs

Aliquots are stored in freezing vials with insert colour coded tops for easy identification when retrieving from the freezers:

Plasma – mauve coloured insert tops

BP – pink coloured insert tops

WBC – white coloured insert tops

NL – grey coloured insert tops

Solutions:

Freezing media

- 70% RPMI 1640, 20% FCS, 10% DMSO
- make daily, leave on ice for at least 5 mins before use
- filter through a 0.22um filter before use, solution must be sterile

Medium

- RPMI 1640, made by media kitchen, in -fridge
- only order and use Fetal Calf Serum that has had QA and shown to be non toxic and supports growth when used on human cells.

Back up of biospecimens

One vial of the WBC/DMSO freeze is to be backed up at:
The Genetic/Epidemiology Department
The University of Melbourne
Parkville, 3050
Contact: Dr Melissa Southey
Tel: 03 8344 4895
Email: msouthey@unimelb.edu.au

Full trays of samples should be taken to the back up site every 3 months.

One Guthrie card made from the whole blood collected from each participant is to be sent as a back up to:

The Familial Cancer Centre Laboratory
Westmead Hospital
Westmead, 2145
Contact: Dr Jenny Leary
Tel: 02 9845 6312
Email: jenny_leary@wmi.usyd.edu.au

In preparing to send the Guthrie cards to the Westmead laboratory,

- place 1 guthrie card per participant into a white envelope.
- label the envelope on the outside with UPN, UFN and the kConFab biospecimen number.
- arrange the guthrie cards in numerical order as determined by the kConFab biospecimen number.
- the envelopes are to be placed in a large plastic box with a secure lid.
- guthrie cards are sent to the Westmead laboratory once a plastic box is full.
- plastic boxes with secure lids can be purchased at all Office Works stores.
- to send the box to Westmead, wrap the plastic box in a large TNT gov bag and place a pre paid 3kg TNT consignment note on the outside of the plastic bag
- addressed consignment note to the Westmead laboratory. Also label the consignment note "Non hazardous – paper only".
- ring TNT on 132 767 for a pick up.
- email Jenny Leary once the plastic box has been pick up to alert her that the guthrie cards are on there way
- guthrie cards are stored in a secure – locked filing cabinet in the Westmead laboratory

kConFab protocol For buccal cell collection

PURPOSE

kConFab participants who don't respond to request to give blood, or firmly refuse the blood collection, should be asked to donate a buccal cell specimen. These cells are derived from the inside of the cheeks and are collected with a simple "swish-and-spit" technique using commercial mouthwash.

SUPPLY FOR COLLECTION KITS:

- 1 small bottle of Listerine (sealed) from Heather
- 1 empty 50 ml tube from Heather
- a plastic biohazard specimen bottle and cardboard box and TNT plastic bag
- a pre-printed return consignment note
- a proforma fax sheet with kConFab ID and name of the participant printed on it

COLLECTION AND STORAGE

A collection kit is given or mailed to the subject along with an instruction sheet (see below). The description of the procedure is self-explanatory. The sample should be sent to PMCI at once for processing, or stored at 4°C until sent.

DIRECTIONS FOR MOUTHWASH

The purpose of this simple procedure is to collect some loose cells in your mouth. It involves the use of diluted Listerine (a commercial brand of mouthwash) that is provided to you in a small sealed bottle to swill around in your mouth to wash off the cells.

Please follow the directions below:

Brush your teeth as you usually do, rinse your mouth well twice with water and wait 2 hours. Do not eat or drink anything other than water during this time.

After 2 hours, pour 10 mls Listerine from the bottle into the tube. Add 10 mls of tap water. Place all of the diluted mouthwash provided into your mouth, without swallowing.

Swish the mouthwash around in your mouth vigorously for 30 seconds. Watch the clock while you do this. It is important that you do not shorten the time you swish the mouthwash, but there is no harm in doing it longer than 30 seconds.

Spit the mouthwash back into the blue top plastic tube. Replace the cover on the tube and screw it on tightly. Place the blue top tube into the plastic bottle, cardboard box and then the plastic TNT bag provided. On the outside of the

plastic bag place the TNT consignment note that has our address pre printed on it.

Please ring TNT on 132 767 within 24 hours after collection for a pick up. Store in the fridge until the sample is collected.

THANK YOU!

EBV cell lines

Transform 1 vial from the stock of WBC/DMSO freezes. The cells to be transformed are determined by the biospecimen committee's priority list. On all index cases transformed send 1 back up flask to GCT at QIMR. Transformations are performed by:

Ms Helen Zogos

The Genetic/Epidemiology Department

The University of Melbourne

Tel: 03 8344 5898

Email: hzogos@unimelb.edu.au

The PMCI central laboratory supplies HZ with pre printed kConFab labels for her to use on flasks and tubes.

Cost as of March 2002: \$57.50/sample

Establishing permanent Lymphoblastoid Cell Lines (LCL's)

CAUTION: All lymphocyte transformations must be performed in PC2 facilities. The technician should wear double gloves whilst working with viable viral supernatants and remove the top pair before leaving the biological cabinet. Plugged tips should only be used during the transformation procedure. This is to prevent aerosol contamination with the viral supernatant. Gloves and all disposable products (including plates and tubes) should be placed in a plastic bag and securely sealed before it is removed from the biological cabinet. All waste must then be discarded in a biological biohazard bag for incineration.

Day 0

Thaw an aliquot of the EBV viral supernatant on ice.

Thaw cells as described in *Recovering Cryopreserved Lymphocytes*.

Spin cells down at 1200rpm for 5min. Discard supernatant.

Resuspend the cell pellet in 200ul of viral supernatant.

Incubate at 37°C for 90min.

Add 900ul of warm RPMI 1640 + 15% FCS + 2% PHA to the cell suspension.

PHA (phytohaemagglutinin) stimulates mitosis in lymphocytes thereby inducing protein, DNA and RNA synthesis.

Add 150ul of the cell suspension to each well in a 96 well plate.

Incubate for 8 days in a well humidified incubator at 37°C, 5% CO₂.

Day 8

Pool 2 of the 8 wells into 1 well in a 24 well plate. Repeat this step for the remaining 6 wells.

Add 350ul of warm RPMI 1640 + 15% FCS + 2% PHA to each well.

Incubate for 4 days at 37°C, 5% CO₂. Freeze 1 vial of cells at this stage

Day 12

Add 750ul of warm RPMI 1640 + 15% FCS + 2% PHA to each well.
Incubate for 4 days at 37°C, 5% CO₂.

Day 16

Examine the plates under an inverted microscope. A successful transformation is evident by the presence of growing viable cells. Typically the cells grow as tight non-adherent clusters of cells, resembling a ball of cells. However, in some instances cells may have not as yet clumped together, instead growing as discrete cells.

Pool 2 of the 4 wells into a T25 flask. Add 2.5mls of RPMI 1640 + 10% FCS. Repeat this step for the remaining 2 wells (this will act as the duplicate for each cell line).

Incubate the cell line (keeping the flask upright as the cells grow in clumps on the surface of the flask), at 37°C, 5% CO₂.

NURSERY CARE OF LCL's

The newly set up cultures are referred to as being in 'nursery care' during the initial stages of generating the stably transformed lymphoblastoid cell line.

Day 20

Remove flasks from the incubator.

To determine whether the cell line requires re-feeding, look at the acidity of the medium and the density of cell clumps. The color of the medium acts as an indicator of the metabolic output of the cells. If the medium is yellow (acidic) and the cell clumps are numerous, the cell line is ready for feeding. Add 5mls of warm RPMI 1640 + 10% FCS to only one of the two flasks. Only one flask of the pair is fed at a time, this is to prevent possible contamination of both flasks at one time.

Incubate the cultures at 37°C, 5% CO₂, keeping the flasks upright.

Day 21

Remove flasks from the incubator.

Add 5mls of warm RPMI 1640 + 10% FCS to the other pair of the flasks.

Incubate the cultures at 37°C, 5% CO₂, keeping the flasks upright.

Day 24

Remove flasks from the incubator.

Determine whether they require re-feeding. If the cell clumps are numerous and the medium is yellow, then add 30mls of warm RPMI 1640 + 10% FCS to one of the two flasks.

Incubate the cultures at 37°C, 5% CO₂, keeping the flasks upright.

Day 25

Remove flasks from the incubator.

Add 30mls of warm RPMI 1640 + 10% FCS to the other pair of the flasks.

Incubate the cultures at 37°C, 5% CO₂, keeping the flasks upright.

Incubate the cell lines until they become confluent, ie. the cell clusters become numerous and the medium acidifies. Disperse the cell clumps by pipetting the cell suspension several times with a 10ml pipette. Take a 0.5ml aliquot of cells from the flask and perform a cell count. There should be $\sim 4 \times 10^5$ viable cells/ml.

Take 5mls of the cell suspension from each flask and place it in a separate 15ml centrifuge tubes. Spin the cells down at 1200rpm for 5min. Discard the supernatant and resuspend the pellet in each tube with 1ml of freezing down solution (FDS). Add the cell suspension to a prelabelled cryotube. Freeze the cells down as described in the *Freezing LCL's*. The cryotubes are labeled with the plate ID, the specimen ID, LCL01 and the date. The two tubes represent the first freeze of each cell line and act as a back up source in case of future contamination. The two tubes are stored at -70°C and their location is recorded in the database.

Potential problems and observations

Some cultures take longer than 24 days to reach confluency (the medium is pink and the clumps few). In this situation, remove 5mls of the spent medium and replace with 5mls of fresh RPMI 1640 + 10% FCS. Incubate until the culture reaches confluency. Replace the spent medium every 2 weeks, if cell growth is slow.

If cultures have not reached a stage where they can be subcultured after 3 months, they are discarded and the transformation is regarded as a failure.

Freeze 4 vials of stock from day 20 onwards on 2 different days.
HT to supply HZ with all bar coded pre printed labels to use on flasks and freezing vials

One confluent flask is supplied to HT. The flasks are:

- split in 1/2 if stock is to be sent onto a researcher as part of a research request.
- The remaining cells (or a whole flask if cells not being sent to a researcher) are washed twice (45 mls) in TE for 5 mins at 1400 RPM.
- Cells are resuspended in 500ul TE and stored in the -70 freezer
- The cell pellet vial is labelled with the UPN, UFN and HZ plate number.
- The EBV cell pellets are kept in a separate storage draw from the whole blood cell pellet
- DNA from the EBV cell pellet is only used after QA between the Guthrie card and the EBV DNA has been performed (please refer to page 5).

For each participant who's WBC's are transformed:

- 10 vials of cells in DMSO are made

- 8 vials are returned to HT. These samples are recorded and their location detailed on the biospecimen database against the relevant participant under EBV Cell Lines.
- If DNA from the EBV cell lines has been made it is logged in the comment box and a separate excell spreadsheet that lists conc of DNA, amount available
- 2 vials are kept as back up with HZ at the University of Melbourne.

Preparation of supernatant for Mycoplasma testing:

- take a 80% confluent flask
- collect 10 mls of supernatant out of the flask
- spin 1000rpm x 5mins
- take 1.5ml of supernatant and place into eppendorf tube
- spin 13,000 x 20 mins
- pour off supernatant carefully
- at this stage pellet can be frozen at -20 until ready to assay
- lyse pellet in protein L buffer and set up PCR reactions

Treatment of Mycoplasma: Plasmocin and it came from Integrated Sciences

Collection of biological specimens

Instructions for Family Cancer Clinic research nurse's

Labelling

Individual and family kConFab ID numbers will be assigned to the KConFab interviewer by Progeny at the time of entering the family history into the database. This number will be written on the tubes, along with the date of blood drawing and the patient's name and date of birth, when the samples are shipped to PMCI or Westmead.

Merged families. Occasionally a family will be "shared" by more than one Family Cancer Clinic and to date it isn't possible for the central registry to merge these families together as one at the central registry. If possible:

- try to generate the UFN and UPNs at one clinic.
- HT and the research nurses can discuss the family involved and who ever made the first approach or has the most family members should be the one to generate the UFN and UPN's.
- If a family has been started by more than one clinic, therefore, 2 or more UFNs generated, please let central registry, central laboratory and the other research nurses involved know of all UFN and UPNs generated for the family.
- Place other UFNs or clinic number on pedigree drawings submitted to the central registry and HT

Blood

1) 20 mls blood in EDTA to be collected for kConFab from every consenting and relevant adult (>18 years) member of the 'fantastic' families requested by kConFab because they fulfill the 'Noosa criteria'.

This means

- i) all alive affecteds (with breast or ovarian cancer)
- ii) all first degree relatives of any affecteds
- iii) all relatives (including spouses) who connect affecteds, even if not first degree

In some cases EDTA blood will also be collected for the NATA-accredited diagnostic lab (this is necessary at least for the youngest, affected in each family), or will have been collected previously - but even in these cases 20 mls kConFab blood (in EDTA) will be collected separately and shipped to Heather.

2) kConFab bloods will be couriered to Heather at the Peter MacCallum Cancer Institute in the approved containers with the pre-paid consignment notes - either from the FCC or from a local GP or pathology office if the blood is collected there (consent will need to be obtained in all cases of course – blood should not be collected until signed consent is obtained). Pathology companies willing to do this gratis will be approached in each state.

Patients who are going to be bled in a local pathology office can be given the Bio Bottle and consignment note, and present a letter to the pathology lab who takes the blood. They will be asked to Fax (proforma fax sheet supplied) Heather Thorne and confirm that the blood is on its way (Heather Thorne will confirm with the RN that the blood arrived safely). For those that wish to be bled by their local GP, interviewer needs to call GP and, using Judy Maskiell's introduction notes, ask if this will be alright. The GP or family member is then sent follow up letter, Bio Bottle, con note, tubes, and proforma FAX to let Heather Thorne know it has been done - and subsequently and TY card from Heather Thorne or interviewer.

Try to collect bloods so that shipments are sent only 2-3 times a week, and not on Fridays. Ideally bloods should be sent within 24 hours, but it can be up to 72 hours if necessary. Keep and ship at room temperature, except in heat waves when an ice pack is recommended.

3) Notify Heather by email (h.thorne@pmci.unimelb.edu.au) and phone/fax of all samples that are shipped, and their numbers, names and dob.

4) TNT are the official carriers of the biological specimens. Once a blood sample(s) are collected, place the EDTA tube into the approved Bio Bottles and place the Bio bottle into the cardboard box and then into the plastic bag that have been supplied to the clinic. On the outside of the plastic bag place a pre-paid consignment note (make sure senders section is filled in) addressed to Heather Thorne, Peter MacCallum Cancer Institute. Ring TNT on 132 767, and inform them of where the sample is to be collected from and the sites telephone number.

5) Monthly report sheets outlining all the material that has been collected and sent to Peter MacCallum needs to be filled in and sent to Heather by the 30th of each month.

6) Empty Bio Bottles will be returned to the clinic for further use.

If the patient really doesn't want to give blood, buccal smears/mouth washes are a alternative. Contact Georgia Chenevix-Trench at 07 3362 0390 for details.

Archival pathological material

Initially, pathology reports will be requested from all tumour material (not just breast cancers) for

- (a) verification of diagnosis and
- (b) confirmation of all breast cancer cases by pathology review.

Informed consent will be obtained for access to this material from the patient, or next of kin if the patient is deceased. The kConFab nurse will then find out where the pathology was performed by asking family members where the surgery was done and obtain the pathology report. These will be sent to Heather Thorne. Batches of pathology reports will be sent to HT each month in express post bags. Please inform HT when pathology is being sent. HT will confirm when pathology reports arrive at PMCI.

NB. The signed consent forms are kept with the research nurses under appropriate security as determined by the local Family Cancer Clinic. Signed consent forms sent to HT are attached to the relevant pathology report.

Frozen tissue:

Although there will not be many opportunities during the kConFab collection period to collect frozen tumour material and prophylactic material, fresh from surgery, such material is invaluable for RNA and protein extraction and so the opportunities are not to be missed. We expect that each collection will be time-consuming, and therefore reduce the amount of time available for other tasks, but it is worthwhile for such useful material. If possible, we would also like to collect 20 mls of blood from all participants who are donating fresh tissue. This can be taken before or at a convenient time after surgery.

If any KConFab family member is known to be having surgery for any known or suspected cancer (or any type), or prophylactic mastectomy or oophorectomy, the KConFab nurse needs to:

- seek permission from the relevant surgeon and determine which pathologist will be used. Send the proforma letter to surgeon with details of pathologist etc and questions re menstrual cycle to be filled in on day of surgery
- if consent was obtained on the old forms which didn't mention prophylactic surgery, re-consent the patient on the new forms to cover this amendment
- notify Heather Thorne of the patient's and surgeon's details
- send copy of the consent form to Heather
- inform the designated pathologist of the patient's name and date of surgery, discuss the protocol for processing the specimen with them, send them a copy if they wish, and warn them that the RN will be bringing the sample to them from surgery (on wet ice)
- determine the source of dry ice, liquid nitrogen and the necessary containers. Liquid nitrogen and dry ice is likely to be available through the

local diagnostic lab attached to the FCC. Discuss with Heather Thorne if there is difficulty in locating these items

- contact the theatre sister to explain the situation, give her the RN's contact details in case of any changes to the schedule, and arrange to collect the specimen from the theatre as soon as it is available. Ask her to fill in the questions re menstrual cycle.
- go to the operating theatre to receive material straight onto ice (as well as pro forma re menstrual cycle questions – fax this to Heather), and then take it immediately to the pathologist. The material will be grossly dissected by the pathologist and examined to exclude occult malignancy, and then cut up and frozen as soon as possible. Tumour material should be cut into 0.5 - 1 cm blocks with a sterile instrument, snap frozen individually in liquid nitrogen and then placed in single layers onto foil in dry ice. For normal breast tissue, identification will be required of portions of the specimen containing connective tissue (as opposed to fat) that is likely to be where the cells of interest are located. Removal of the (yellow) fat as far from possible from the (white) connective tissue is preferable. This should be done before cutting the tissue into 0.5 cm pieces and freezing as above.
- make sure there is sufficient dry ice covering the sample to keep it frozen – for overnight shipment 3.5-4.0 kg dry ice is needed, and it is essential to use the well insulated eskies in which enzymes are shipped, instead of the smaller ones with a string handle. Any lab should be able to find a suitable esky for this purpose.
- On the day of shipment from all sites within Australia, ring Blair at Blue Circle Melbourne on 03 9258 6042 and book the shipment. Request that collection of dried ice shipment be mid afternoon at your site and delivered by 10am at Westmead Hospital the following day. Use Blue Circle next-day delivery consignment notes as supplied and addressed to:

Specimen Reception,
Level 2,
Peter MacCallum Cancer Centre
East Melbourne, 3002

Label the con note as follows:

'Dried Ice UN1845' under the description of goods
add Blue Circle black sticky note

11. notify Heather (by phone and email with copies to Lisa and Danni in case she is away) of its imminent arrival and consignment number, booking number and flight details and ask for confirmation of its arrival

Phone Heather – 03 9656 1542
FAX Heather – 03 9656 1457

Email Thorne Heather <heather.thorne@petermac.org>
cc to "Daniella Surace (E-mail)" <d.surace@pmci.unimelb.edu.au>

12. Blair will confirm with you the next day what time the esky was delivered at Westmead and who signed for the esky.

13. In some cases, as with remote regions, it is not possible to obtain fresh tissue and transport the material on dried ice. In these cases please contact HT who will supply the surgeon/pathologist with a tube containing RNA $later$, instruction notes, a bio bottle and pre paid consignment note addressed to the Westmead laboratory. This is the least preferred collection treatment of fresh tissue but we would rather obtain fresh tissue in this way than not obtain any tissue at all. RNA $later$ can be stored and transported at room temperature. Once tissue is placed into RNA $later$ tubes can stored at 4 -10C. When transporting to Westmead Hospital, place an ice pack into the bio bottle.

14. EDTA tubes, empty bio bottles, plastic bags, pre printed and blank consignment notes, stamps and pre printed reply paid envelopes will be supplied by the central laboratory at PMCI on request.

Check Sheet for DNA handling

This check sheet has been developed to maximise the use of made DNA, and, to avoid sample mix up. Should sample mix up occur we need to be able to track all aliquots in storage back to the specific research project that DNA has been supplied too.

Making DNA:

1. When transferring to another tube, always cross check that the numbering on the 2 tubes is the same.
Only work on 12 DNA at any one time.
Take a break between batches
2. It is practical to take the DNA out of the -70 in numerical order. Before you start extracting the DNA, “shuffle” the BP tubes up so that none of the biospecimen numbers are in the same numerical range.
Work off a logical grid when aliquoting, ie, if you have a list of DNA, set the DNA to be aliquoted in the same order as your request sheet.
3. Label all DNA with the date that it was made
4. If there are 2 DNAs tubes in storage, record on your work sheet the date of the DNA that you used. In the new database there will be provision for the recording of this date on the work and job sheet.
This work sheet could be the agarose gel grid sheet or the running UPN work sheet.
It is important to have these details as a hard copy sheet plus entry on the database.
5. If there are 2+ tubes of DNA in storage – how to handle?.
 - Best not to pool DNA tubes
 - Try not to leave DNA in storage for too long as with time it may degrade.
When you are working on a new request, check first to see if you have enough DNA available in existing DNA tubes before making a fresh batch of DNA from the BP.
 - If you do need to pool DNA (and will might have to in some situations) record on your work sheet that this has been done, and, as protection, take 5 ul from all pre pooled tubes and QA against Guthrie QA

kConFab : Frozen Tissue Bank Protocol – receipt and storage

Access and Procedure Policy:

- one person designated to manage the tissue bank
- that persons name must be logged on the hard copy report sheets and in the database for every aspect of transaction: receiving tissue, retrieval for QA, retrieval for research project
- all information related to the collection and receipt of tissues must be keep in a plastic pocket for each participant, transit labels, email correspondence
- only one tissue to be worked on at any one time
- tissue bank up to be at Westmead Sydney. If enough tissue is received, the material will be split into 2 vials with each vial being stored in 2 different LN vats at PMCC until 5 full boxes are ready to transfer to WM for the back up. The dry shipper will be used for the transportation of the tissue.
- tumours will undergo QA before normal tissue and mutation positive normal tissue before mutation negative

Scope of the protocol:

This protocol is designed to cover all aspects of the receipt of preliminary evaluation of and storage of the human material collected by kConFab and held in the research department at Peter MacCallum Cancer Centre. In addition the protocol covers all aspects related to the maintenance of the resource inventory through electronic and hard copy record management, audits and QA.

Note: A staff must be trained in the safe use of handling and transportation of biological material and liquid nitrogen before working with the resource as outlined in the Peter MacCallum Cancer Centre safety manual.

Tissue Collection – fresh frozen and RNAlater

1. The RNs will notify the PMCC central laboratory (Danni, Heather and Lynda) as soon as possible about upcoming tissue collections. The RN will confirm with all laboratory PMCC staff when the tissue has been collected and the scheduled delivery day to PMCC along with the con note and booking number. Notification is essential with several laboratory staff to ensure availability of staff to receive the shipment. As all deliveries are made to the main level 2 research reception desk, it is essential that office staff members are informed about in coming shipment the day before the scheduled delivery, and, they know the importance of notifying the laboratory staff as soon as the delivery arrives.
2. Fresh frozen tissue collected by the RNs will now be placed in histocassettes, not foil. HT will supply the histocassettes and biopsy pads to be used to all of the RNs. The use of histocassettes and biopsy pads will stop:

- large pieces of tissue being snap frozen which leads to,
 - poor preservation of the tissue. Pathologists recommend 3mm tissue pieces. This size is a good fit in the histocassette, and,
 - extra handling of the tissue at the central laboratory due to further dissection of the tissue into smaller pieces. Extra handling and cutting of the tissue at the central laboratory has the risk of exposing the tissue to higher temperatures than recommended
 - When accessing the tissue for QA or research projects, “flipping” the frozen tissue out of the histocassette is an easier process than removing tissue from foil.
 - The use of the biopsy pads placed inside the histocassette results in a “flat” surface that is essential when mounting the tissue onto the disk to cut for frozen sections.
 - With foil, proteins stick to the foil that makes removal of the tissue difficult, and at times the foil becomes embedded in creases or folds of tissue if the tissue is not wrapped completely flat. Wrap single or multiple *labelled* histocassettes in foil, label UPN/UFN around the outside and store in LN. This will help eliminate dehydration of tissue.
 - *QA. We will place a histocassette in LN for at least 6 months (April – September 2004) to determine long term effect of LN temperatures on the histocassettes.*
3. Noel from Blue Circle will confirm with the RN the next day what time the esky was delivered at PMCC and who signed for the esky.
 4. PMCC laboratory staff will email the RNs to confirm that the tissue has arrived.
 5. If tissue hasn't arrived by noon, laboratory staff should contact Blue Circle to track down the delivery.
 6. PMCC staff member in charge of the tissue bank needs to make sure all resources and equipment is in place before tissue is processed; LN, clean sterile surgical equipment, cutting plate, weigh boat, histocassettes, dry ice, dry shipper. After use, all equipment must be decontaminated and autoclaved as detailed in laboratory manual.
 7. It is essential that the laboratory staff never let the temperature of the tissue *rise above* the temperature of LN.
 8. When the PMCC laboratory staff member starts processing the tissue:
 - UPN/UFN, name, DOB accompanying the shipment must be cross-checked with the identifiers supplied by the RN via email and the kConFab database
 - All fields on the hard copy tissue report sheet must be filled in. Comments section can contain delivery problems, state of material on delivery, tissue specific problems such as tissue lying on top of dry ice rather than being buried
 - One piece of tissue is to be placed into a histocassette. *If the material arrives in RNA later, make sure to trim as much fat off the specimen as possible.* The histocassette(s) must be appropriately labelled eg FTR1/UPN/UFN/initials **on both sides**. The histocassette(s) are then placed into a Nalgene tub (or if multiple wrapped

in foil) that has a UPN/UFN/initials label stuck on the outside of the tub and a free floating label inside the tub.

- If two or more tissue arrive with out identifiers left and right, tissue piece are to be numbers 1, 2, 3.
- As soon as the housekeeping issues such as recording number of pieces received and weight of tissue is completed, the tissue must be placed immediately in the permanent LN vat, level 2. Location of Nalgene tub recorded on tissue report sheet.
- On the same day, the staff member handling the tissue must enter into the kConFab database “tissue field” all of the information recorded on the hard copy report sheet.
- If the pathology report related to the tissue collection has not been sent to the central PMCC laboratory within 7 working days, the PMCC laboratory staff member will remind the relevant RN about getting a copy of the report and passing onto the central laboratory.
- Only one tissue must be worked on at any one time.
- Documentation about each tissue collection is placed in its own plastic pocket in a dedicated folder where report sheet, email correspondence, con notes and any other correspondence related to that tissue collection is to be kept

9. For tissue collected into RNAlater, RNs are supplied with 10 ml greiner tubes with 6 mls of RNAlater. If a large amount of tissue is available at the collection site, extra tubes must be used to accommodate the tissue. Once the tissue in RNAlater is delivered to the laboratory, the tissue is dissected into the appropriate size (3mm) and placed into appropriately labelled histocassettes before snap freezing and storing in LN. The same protocol and **tissue report sheet** is used for RNAlater collections. On occasions, the tissue collected will need to be further dissected at the central laboratory, especially those collected into RNAlater if they are to large to fit into the histocassette, fatty etc. If in doubt about the dissection, a Pathologist must be consulted.

10. *If there is an abundance of tissue collected a portion of this material will be fixed. This will be a joint decision made by HT and the designated tissue bank manager. Any tissue collected into formalin must be removed from the fixative after 24 hours. As soon as tissue is placed into fixative, the material can be taken to histopathology at PMCC so that it can be processed under clinical processing conditions.*

Frozen Tissue Bank Protocol – Tissue removal and characterization:

The aim of this process is to:

- characterize all stored frozen tissue
- the characterization of tumour (any type) is given priority in each batch
- a thin, frozen full face section is cut, H&E stained, reviewed and scored on the research pathology sheet developed by Paul Waring. *A different score sheet is used for prophylactic review to tumour review please see score sheets below.*
- the research pathology report needs to be entered on the database under “research pathology”.
- ***It is essential that the tissue isn’t out of LN for more than 3 minutes***

Removal of tissue from storage:

1. For each batch to be characterized, a list needs to be generated prior to retrieval from the permanent LN vat that lists the tissues and locations of the tissue. 10 different tissue collections can be retrieved and characterized at one time. Tissue to be characterized can be placed in the dry shipper, on hold, until cut.
2. When each tissue is retrieved, for each tissue:
 - the hard copy histology request slip must be used
 - all fields must be filled in on this hard copy sheet detailing UPN and the code for every tissue to be characterized
 - all fields must be filled in about retrieval of the tissue on the kConFab database
 - *record the time taken to cut a section, and time taken to return the tissue to the dry shipper to LN*
3. When cutting a frozen sections – *Tumour sample:*
 - 1 thin section is cut and used for [H@E](#) review. Slide is labelled with the UPN and L1 to indicate the level 1 cut of the tissue
 - 5 thick sections (10 um) are cut rolled into a screw top cryovial tube. This is a ready source of material pre cut for research projects and eliminates that concern by the PMCC histology manager of bring the tissue up to –20 every time frozen sections are required.
 - the eppendorf tubes are labelled with UPN/UFN/initials and given to the histology manager before he starts cutting frozen sections
 - location of the eppendorf tubes and H&E slides is recorded in the kConFab database
 - 1 thin section is cut at the end of the process so that “book end” sections are available for review. This [H@E](#) slide would be labelled with the UPN and L2 to indicate the level 2 cut of the tissue.
4. *When cutting a frozen sections – Normal sample:*
 - It has been found that frozen normal breast tissue, with a large component of fat present, is extremely difficult to cut and shatters easily. *If you start cutting and you find the tissue difficult to manipulate, stop cutting and place the material back into the LN vat, QA will not be performed on this sample until it is requested for a specific research project.*
5. Batches of H&E slides to be given to Paul Waring to review. Update the research pathology review onto the kConFab database as soon as possible.
6. Place the frozen tissue back into the permanent LN vat storage space and update all listed fields on the kConFab database immediately. Allocate and record the position of the cryovial tubes.
7. *For specimens where there is enough material, 2 aliquots will be stored. One vial in the kConFab and one in the AOCS LN vat. When 5 boxes are filled with tissue, the vials in the AOCS will be shipped to the tissue bank at Westmead as the tissue back up.*

Audits and QA:

- *Every 6 months a vertical audit of the facility will be conducted. A member from the PMCC tissue bank or AOCS will randomly select UPNs from the “tissue field” screen and note the position of the tissue. They will then go to the LN vats and cross check that that designated tissue is in the location as detailed, and the numbering of the vial (s) is correct.*
- *When we have a fresh tissue collection and there is an abundant amount of material available (preferably normal and tumour) do a time course to access:*
 1. *how long it takes to cut a frozen section – record the time*
 2. *double the triple this time between cutting a frozen section*
 3. *extract RNA from the sections and determine the amount and quality of RNA*
 4. *place the remaining tissue back into LN vat for 2 weeks, remove tissue and repeat step 1-3.*

Send away:

All fields listed on the database must be filled in a record what type of tissue and how much was sent to whom. It is recognised at this point that this section will develop further once tissue is being provided for research projects.

Form to be used with every tissue collection:

Hard copy tissue report sheet for all fresh tissue/RNAlater collections

Name of participant:

UPN/UFN:

Date of collection

Date of arrival in the laboratory

Date processed by laboratory

Collected/Sent by kConFab staff member (initials)

Type of tissue:

Exact number of pieces and the numbering of each piece:
(record size and weight of each piece of tissue)

LN vat location and date placed in LN

Pathology obtained: Y / N

Comments:

Note:

- All items on this sheet must be entered on the database the same day tissue is processed, even if incomplete
- Update pathology report into the database the next week. Remind the RNs if pathology report hasn't arrived at the lab.
- If no UPN/UFN available when tissue collected, prompt the RN the next week to issue the number

Processed by: initial

Research Pathology Review Sheet for Tumours

kConFab PERSON ID

SLIDE REVIEW

PATHOLOGIST

DATE

LAB

SPECIMEN ID

GRADE

WELL DIFFERENTIATED
MODERATELY DIFFERENTIATED
POORLY DIFFERENTIATED

UNDIFFERENTIATED
NOT DETERMINED/STATED

SILVERBERG

ARCHITECTURAL PATTERN
NUCLEAR PLEOMORPHISM
MITOTIC ACTIVITY

IMPORTANT INFORMATION

0 – 25% 25 – 50% 50 – 75% 75 – 100%

NEOPLASTIC COMPONENT

0 – 25% 25 – 50% 50 – 75% 75 – 100%

NON-NEOPLASTIC COMPONENT

LYMPH

0 – 25% 25 – 50% 50 – 75% 75 – 100%

STROMA

0 – 25% 25 – 50% 50 – 75% 75 – 100%

NORMAL COMPONENT

TYPE

0 – 25% 25 – 50% 50 – 75% 75 – 100%

TYPE

0 – 25% 25 – 50% 50 – 75% 75 – 100%

NECROTIC COMPONENT

0 – 25% 25 – 50% 50 – 75% 75 – 100%

Morphology

Research Pathology Review Sheet for Normal - Prophylactic specimens

kConFab PERSON ID

SLIDE REVIEW

PATHOLOGIST **DATE**

LAB **SPECIMEN ID**

GRADE

SILVERBERG

ARCHITECTURAL PATTERN _____
NUCLEAR PLEOMORPHISM _____
MITOTIC ACTIVITY _____
CELLULARITY _____

IMPORTANT INFORMATION

NEOPLASTIC COMPONENT

0 – 25% 25 – 50% 50 – 75% 75 – 100%

NON-NEOPLASTIC COMPONENT

LYMPH
 0 – 25% 25 – 50% 50 – 75% 75 – 100%

STROMA
 0 – 25% 25 – 50% 50 – 75% 75 – 100%

NORMAL EPITHELIUM COMPONENT

TYPE _____
 0 – 25% 25 – 50% 50 – 75% 75 – 100%

DUCTAL COMPONENT

TYPE _____
 0 – 25% 25 – 50% 50 – 75% 75 – 100%

NECROTIC COMPONENT

0 – 25% 25 – 50% 50 – 75% 75 – 100%

Morphology

Research Pathology Review Sheet:

**NORMAL – PROPHYLACTIC OOPHRECTOMY SPECIMENS
kConFab PERSON ID**

PATHOLOGIST **DATE**

SPECIMEN ID

Ovary **Left** **Right** **Bilateral**

EPITHELIUM

SURFACE EPITHELIUM

Absent Present - Scant Moderate Abundant

SURFACE EPITHELIUM – PAPPILATIONS

Absent Present - Scant Moderate Abundant

EPITHELIAL INCLUSION CYSTS

Absent Present - Scant Moderate Abundant

CORTICAL INVAGINATIONS

Absent Present - Scant Moderate Abundant

OTHER ELEMENTS

STROMA

Absent Present

CORTEX - FOLLICLES

Absent Present

CORTEX - CORPORA LUTEA

Absent Present

FOLLICULAR CYSTS

Absent Present

RETE OVARIUM

Absent Present

FALLOPIAN TUBE

Absent Present

MORPHOLOGY

Well preserved Moderate preservation Poor preservation

COMMENTS

Who to request a blood sample from and who to interview

The following instructions are used by the kConFab research nurses. Adults, male and female, over the age of 18 are eligible to be recruited.

NB. Individuals can still contribute to the study even if they do not wish to give blood, or do not wish to know the results of any genetic testing.

FIRST, chose the family contact person (FCP), who should be an adult female with at least one affected first or second-degree relative. She will be the person who will initially approach other members of the family to be involved, so great care should be taken in making sure she is prepared and capable of acting as the initial route into the extended family. She may or may not be affected, and need not necessarily be the “consultand”.

1, for each FCP, request a blood sample and interview, irrespective of cancer status.

2, Fill out the family history chart by asking the FCP about all first and second-degree relatives, as a minimum. More relatives may be entered on the family history chart, and the status of relatives may be updated or changed at later stages (please see below point 3).

Definition of an **Affected Individual**

- breast cancer (in a male or female), or
- ovarian cancer

(This definition could be changed following in-the-field experiences)

3, For each adult affected relative of the FCP identified in 2,
(a) request blood and interview,
(b) request blood from and interview all adult first-degree relatives. If needed, extend family history chart to include any such relatives not already on the chart.
(c) If any adult children are studied as part of (b) above, request blood from and interview the (blood) father, or mother, of those children, if not already studied.

4, If any of the newly studied (adult) members in 3 are affected themselves, request blood from and interview their first-degree relatives following the same procedure. Repeat this procedure if more affected relatives are identified.

5, Review pedigree. Try to ensure that blood is sought from all individuals in direct ancestral line between affected individuals.

NB. If a subject to be interviewed is deceased or cannot be interviewed (i.e. refuses, or is unable to be contacted), arrange for a proxy interview using the

closest relative selected in the following order: spouse, first degree, second degree.

*Also, if a participant doesn't wish to give a blood sample, a mouth wash specimen can be obtained. Please refer to mouthwash protocol under **Laboratory Protocols** page 12-13*

This is a copy of the proforma fax sheet that is used when sending blood to PMCI:

kConFab letterhead

Clinic telephone number -----

TNT Consignment note #-----

Thank you for offering to collect a blood specimen for us from your patient(s). The specimen will be used for national project (kConFab) researching familial aspects of breast cancer. We have an arrangement with TNT who will collect the specimen from your premises.

1. Place the 18 mls of blood into the EDTA tubes provided and label the tube with name and date.
2. Place these tubes into the orange topped bio bottle into the cardboard box and plastic bag for safe transportation. Keep these tubes at room temperature, although if the temperature is over 30C please place an ice pack into the bio bottle.
3. Place the supplied pre- paid TNT consignment note on the outside of the plastic bag (with bio bottle containing blood specimen inside). The consignment note should be addressed to:
Ms Heather Thorne
Research Department, Peter MacCallum Cancer Institute, Melbourne
St Andrews Place, East Melbourne, 3002
4. Ring TNT pick up on 131 150, inform them of your address and telephone number and that you have a "biological specimen" for collection with a "pre paid" consignment note.
5. Please fax through this sheet of paper with the name of the specimen(s) taken and date.

Name of Patient:_____UPN-----UFN-----

Date specimen taken:_____

Could female participants please answer the following 5 questions:

1. Are you currently pregnant? Yes or No (please tick correct boxes)
2. What was the date/month when your last menstrual cycle started?.....
3. What is the average length of your menstrual cycle?.....days
4. Have you gone through/are you going through menopause. Yes or No
5. Are you taking the oral contraceptive pill at present? Yes or No
If not, did you stop taking the oral contraceptive pill in the last 3 months? Yes or No

**FAX this sheet with the details of specimens being sent to
Heather Thorne
at the Peter MacCallum Cancer Institute, Melbourne
FAX Number 03 9656 1457**

Thank you for your co-operation. Should you have any questions or concerns please contact Heather Thorne (telephone 03 9656 1542).

Recording of collected specimens

All biospecimens collected (blood, mouthwash) have a UPN and UFN number that is generated by Progeny at the local clinic where the participant/family was recruited and consented. As mention above, when blood or mouth washes are collected, the research nurse emails the PMCI central processing laboratory to say that blood is on its way with details of name, DOB and UPN/UFN for each participant, and/or, the private pathology centre or GP office fax through the profoma fax sheet to the PMCI central laboratory to alert them that a biospecimen has been collected and being sent.

When blood or mouth washes arrive at the central processing laboratory at PMCI the following recording procedures are performed:

- (a) biospecimen(s) (blood or mouthwash) are taken out of the bio bottle
- (b) name, DOB, UPN/UFN written on the blood tube are checked against details on RNs email and/or proforma fax sheet
- (c) participants following details are recorded in a hard copy red book. To date, these books are numbered 1-4. The PMCI biospecimen number allocated for the first specimen to arrive at the PMCI processing laboratory was #1, consecutive numbers have been generated for each biospecimen that has since arrived.

Clinic #	UPN	UFN	Name	PMCI Bio #	DOB	Date sent	Date arrive	Amt Rec'	# Guthrie cards	# Plasm	# W B C	# N L	# BP

- (d) comments are also recorded about delays in transportation of blood, strange appearance of sample and any other unusual occurrence or observation.
- (e) Blood is processed into fractions as detailed in the biospecimen protocol page XXX.
- (f) Once the biospecimen is processed and stored in appropriate freezer and/or plastic storage boxes, the laboratory staff member who did the processing that day emails the research nurse at the local clinic that arranged for the biospecimen to be collected – recruited the family.
- (g) The laboratory staff member informs the research nurse that the biospecimen arrived safely, the date that the biospecimen was collected and the date that the biospecimen arrived. The research nurse in each clinic logs the date that the specimen was collected and arrived at the processing laboratory onto the FBI database that they use in the clinic.
- (h) The laboratory staff member also writes in the email the participants name, DOB, UPN and UFN so that the research nurse can double check that the details supplied on the blood tube, previous email or proforma fax sheet is correct about each participant.

- (i) Either at the end of each day after biospecimen processing is finished or on a Monday when it is unusual to receive biospecimens, all new entries in the hard copy red book and logged onto the biospecimen database.

Recording and auditing of fresh tissue collections

Fresh tissue (breast and/or ovarian), from prophylactic surgery or surgery for suspected tumour is collected by the research nurse from consented participants. Please refer to **Collection of Biological Specimens** page 18-22 for collection details.

- Once the fresh tissue has been collected and delivered safely to the Westmead laboratory, the research nurse obtains a copy of the pathology report related to this surgery and a copy of the mutation test result, if one is available, and sends a copy of these reports to HT, usually in batches each month in express post bags.
- The pathology report and mutation test result are logged against the relevant participant on the PMCI biospecimen database. All tissue that has been sent to Westmead is also recorded on the Westmead laboratory tissue database.
- Once a month an audit is performed between HT and the Westmead laboratory on tissue collected. HT sends to the Westmead laboratory a copy of the relevant pathology and mutation test results in express post bags.
- HT emails Westmead to alert them that reports are on their way. Westmead confirm when the reports have arrived safely.
- The UPN, UFN and biospecimen number is written on each report.
- Sometimes there is little warning about fresh tissue collections, therefore, names and DOB are the only identifiers sent to the Westmead laboratory with the tissue. The research nurse updates HT and the Westmead laboratory asap with the assigned UPN/UFN.

Storage of biospecimens:

As mentioned above in **Recording of Collected Specimens** page XXX, biospecimens are given a consecutive PMCI biospecimen number when they arrive at the laboratory prior to processing. All biospecimen aliquots/fractions are stored according to the PMCI biospecimen number in the -70 freezers and liquid nitrogen vats. Details for the exact location for each fraction/aliquot in freezers and liquid nitrogen vats can be found linked to each participant on the biospecimen database.

Security of biospecimens

All -70 freezers and liquid nitrogen vats that hold kConFab material are locked with keys. kConFab does not share any freezers with any other research group at PMCI. Only approved kConFab laboratory staff know where the freezer keys are kept and have access to the storage facilities.

Security of biospecimen database

The biospecimen database is password protected and kept in the kConFab office. Only approved kConFab staff members know the password to gain access to the database. The biospecimen database is back up each night onto the local research server which is fire walled off from the main hospital. The back up of the database on the research server is also password protected.

Security of the hard copy entry book

The hard copy red book that lists all biospecimens received is locked each evening in a filing cabinet in the kConFab office. Only approved kConFab staff members have access to this key and the filing cabinet.

Pathology

Accessing pathology reports

On all consented kConFab participants, the research nurse will try to verify all reported cases of cancer, not just breast and ovarian cancer in the family. Verification should be done on living and deceased family members. kConFabs preference for the type of report for verification purposes are ranked in the following order:

- (a) pathology report
- (b) verification from a cancer council or AIHW
- (c) death certificate
- (d) if self reported and no formal reports are available, please use the John Hopper verification form (HT can supply)

Calling in pathology slides and blocks

Histopathology requests should be handled by the central laboratory. This ensures that a centralised recording is kept on what is called in, what is received, who it is sent to for research investigations and when it is returned to the original pathology laboratory. In calling in histopathology, ring the laboratory manager at the site detailed on the pathology report. Explain request and immediately fax through to the manager a copy of:

- participants signed kConFab consent form. If HT doesn't have a copy of the participants consent HT will call it in via the research nurse.
- Copy of the original path report
- a covering letter explaining exactly what is required.
- on the covering letter list all block(s) and / or slide(s) number as detailed on the pathology report

Log onto the biospecimen database:

- what has been received - date received
- all material that has been sent to researcher(s)
- supply covering letter (with date) to the investigator with full details of what material has been sent to them

Return of block and slides

Log on the biospecimen database

- the date slide(s)/block(s) returned from the research laboratory to the central laboratory at PMCI
- date sent back to original laboratory
- when returning supplied material to the original laboratory send covering letter thanking the laboratory for being willing to co operate, use kConFab letterhead

Accessing mutation test results

On all consented kConFab participants, the research nurse will liaise with the Family Cancer Clinic staff to determine if clinical predictive mutation testing has been performed as part of the Family Cancer Clinic Service. The mutation test report can be obtained from either the local Family Cancer Clinic file, or, with approval from the Clinic Head and the senior scientist at the local testing laboratory files

Sending of mutation test results and pathology reports to PMCI

All mutation test results and pathology reports obtained by the research nurses are sent to HT at PMCI. It is requested that

- UPNs and UFNs are written on the top of all reports by the research nurses before sending.
- all reports can be sent in batches each month in express post bags.
- HT will supply express post bags to the research nurses on request.
- research nurses should email HT when they express post all reports and inform HT that the reports are on their way.
- research nurses should keep the sticker with the express post bar code as a reference until the post arrives safely at PMCI
- HT will confirm via email to the research nurse that the express post bags with reports has arrived safely

Handling and Storage of mutation test results and pathology reports

Pathology reports:

When pathology reports arrive at PMCI, they are logged onto the biospecimen database as having been received and logged against the individual as described. The UPN and UFN written on each report by the research nurse is checked against the biospecimen database for accuracy. The kConFab biospecimen number is also added to each report, next to the UPN and UFN and the pathology reports are then filed in consecutive numerical order as determined by the biospecimen numbering system.

Security:

The filing cabinet where the pathology reports are located are locked and access to the filing cabinet is only available to approved kConFab personal. The key to the filing cabinet is kept in a secure location and only known to approved kConFab personal.

Mutation test reports

When mutation test reports arrive at PMCI, they are logged onto the biospecimen database as having been received and logged against the individual as described. The UPN and UFN written on each report by the research nurse is checked against the biospecimen database for accuracy. The kConFab biospecimen number is also added to each report, next to the UPN and UFN. Mutation test results are filed in clinic folders
ie all PMCI mutation test results are kept in one folder.

Security

The filing cabinet where the mutation test reports are located are locked and access to the filing cabinet is only available to approved kConFab personal. The key to the filing cabinet is kept in a secure location and only known to approved kConFab personal.

Application to access kConFab biospecimens and or data

Researchers can approach kConFab for access to biospecimens and/or data. Before any kConFab biospecimen or data is sent to a researcher(s) the following documents must be read and filled out by the researcher(s) involved:

Information, Policies and Procedures for Access to Biospecimens
and

Data Request Form

The 2 documents mentioned above are available via the home page at:
www.kconfab.org

Proof of ethics clearance from the relevant ethics committee, peer review and proof of funding are essential before any application will be approved by the relevant kConFab sub committee and executive committee.

When a research project is approved, HT writes a letter to the researcher stating the project is approved, who to contact for the material that is required and mentions that an annual report is required for the executive committee to review.

**Assessing pilot and full applications
kConFab Biospecimens Committee
Scoresheet for Pilot and Full applications**

Title:
Applicants:
Institution:

Scientific aims	outstanding	novel	important	reasonable	confirmatory	Weak/uncle:
Feasibility of pilot	Assured	Likely to be feasible	Might be feasible	Will yield data without advancing aims	Unlikely to be feasible	No chance
Group credentials/track record in this type of research	outstanding	excellent	very good	good	average	poor
Justification for amount of material requested	satisfactory	not satisfactory				
Ethics approval	Yes	No				
Does the overall merit of the request justify the granting of material?	Yes	No				

Biospecimen Committee member:
Date:

Tracking of biospecimens

At present some of the biospecimen material sent to researchers with approved kConFab projects can be logged onto the biospecimen database. As a back up, until the biospecimen database is further developed, all material sent to researchers is also logged onto an excel spreadsheet. A covering letter generated from a word file with full details about material supplied is included with the material when it is sent to the researcher(s).

kConFab also provides DNA for haplotyping and spreading analysis. Samples to be used for this analysis are determined by the relevant sub committee (mutation and family review sub committee). The central laboratory liases with the 2 sub committees to determine how much DNA is to be supplied and appropriate QA strategies.

Protocols when updating Participant Information

For all of the updates listed below in section A, B, C, D and E, please date all work sheets when you receive new information and date the work sheets when action has been taken

A: Protocol for updated address

It is important to have updated and correct participant addresses at the central registry as all 3 kConFab research projects need to contact participants from time to time.

All address updates need to be entered by the local RN onto the FBI database.

Addresses that need to be updated by the RN onto FBI can come from:
Personal communication from a participant or family member to the local RN.
Record/date when informed of updated address

Notification about a change of address after personal communication or a returned change of address form from a participant or family member involved in the clinical follow up or psychosocial project.

In this situation all notified change of addresses will be entered onto a work sheet, along with name, UPN/UFN and passed onto the RN

The research team will record the date on the work sheet.

If there are nay problems with names/addresses refer immediately back to the central registry

It is suggested that these address update forms be stored in the front of the RNs family folders for easy reference.

This information will be sent to the local RNs in batches.

Notification about a change of address after a newsletter mail out which contains a change of address notification form and reply paid envelope.

In this situation all change of address notifications are sent back to HT. Date of update recorded on the change of address sheet

HT will pass the forms onto SP/EN who will verify name and address against the central registry records, add UFN to the top of the notification form and then send to the local RN for the update to be performed

RNs - If the UFN is wrong and the participant doesn't belong to your clinic, please discuss with the central registry staff Sandra and Eveline.

B: Deceased Participants.

- If a family member informs the RN about a death within the family, the RN should update the FBI database in regards to that participant and verify the reported death (cancer) and pass reports onto HT

- When a member of the research team obtains information about a deceased participant from any of the sources as described above in **A**, all information about the participant will be recorded, UPN,UFN name, DOB, dated

by the research team and this information will be passed onto the local RN to update the FBI database. If cause of death was cancer, pass verifications onto HT

- Keep a copy of the sheet passed on by the research team in the front of the family folder – date when action taken

C: Tracking down “Lost” Participants

Despite every effort, occasionally the research teams have trouble locating a participant using the supplied contact details. The kConFab ethics committee has granted approval for the local RNs to contact a close family member if all other avenues trying to find a participant have failed.

The kConFab ethics committee realise that:

the RNs will have to use their judgement in choosing the most appropriate person to contact

care will need to be taken so not to reveal “to much” or the real reason you are trying to locate someone. Confidentiality of all individuals in the project must be observed at all times.

Who is and isn’t involved in the research study must not be revealed to other family members.

updating the kConFab mailing list for the yearly newsletter is a good excuse as to why you are trying to track down a “lost” participant. Spiel available if needed if talking to a family member also ask if anyone else has moved recently, including spouse, children.

the kConFab consent form will be submitted to all local ethics committees soon with an amendment which requests that we collect the name of a close friend, in addition to a family member, on the consent form should a participant be lost to follow up.

D: Clinical Follow up – report deaths

When developing the clinical follow up questionnaire the following questions in section **D** and **E** were included to assist the core project about new cases of cancer (specifically breast /ovarian cancer) and deaths:

“ D2 – Has anyone in the family died during the last 3 years?

Name, relationship, cause of death and data of death are recorded.

The clinical follow up team will:

photocopy the page that details this information

add the UPN/UFN of the participant supplying the information and pass the sheet onto the local RN. Sheets will be dated by the research team

On investigation by the local RN, the nominated deceased person (name is supplied) **may not** be a kConFab participant and not informative for the project.

If this is the case no further action is required.

If the nominated person is a kConFab participant, please update the FBI database and pedigree drawing. Verify death if death was due to cancer. Send verification document onto HT

If the nominated person is **not** a kConFab participant but is informative for the project, the RN should check the local records about this family. If this person had never been approached, approach spouse or next of kin, gain proxy consent and proceed as normal. If the records show that this person had been approached in the past and refused to participate in the project **no further action should be taken** other than to update the pedigree drawing in a de identified manner. (This needs to be monitored)

E: Clinical Follow up – New reports of cancer

When developing the clinical follow up questionnaire the following question was included to assist the core project:

D1 “During the past 3 years, has anyone in the family, who is related to you by blood, been diagnosed with a new cancer of any type”. Relationship and cancer type recorded (not names).

The clinical follow up team will:

photocopy the page that details this information

add the UPN/UFN of the participant supplying the information and pass the sheet onto the local RN.

The RN needs to telephone the person who supplied the information.

It is suggested that the RN have a pedigree drawing of the family in front of them when they ring to help recognise and locate the person who has been nominated. There maybe overlap of information supplied by different family members. There maybe a “self” report and also the same update from 2-3 other family members. For this reason it is advised to have dated work sheets in front of you to cross-check against

As above in section D, the nominated person **may not** be a kConFab participant and not informative for the project. If this is the case no further action is required.

If the newly diagnosed person is a kConFab participant, contact the person directly and ask if they are happy to update their cancer history. Obtain verification reports, update FBI and pass reports onto HT.

If the newly diagnosed person **is not** a kConFab participant but would be informative for the project, has not been approached before, nor refused to be involved when approached previously, treat the person who has supplied the information like a FCP. Ask if she/he would be willing to approach this nominated person to see if they would be interested in being involved in the project. Proceed as normal

If the newly diagnosed person **is not** a kConFab participant and has been approached before and refused to participate **no further action should be taken.**

In the pilot study the person who nominated the newly affected did ask the person again if she wanted to be involved – the nominated person was still not interested in being involved. The message here is to tread carefully.

Some newly affected nominated persons are already part of the study and have either been followed up by the clinical outcome or psychosocial team or will be in the near future.

Family Review
May 2003
Georgia Chenevix-Trench

**NOTE – FAMILY REVIEW IS ON THE BASIS OF REPORTED
CANCERS AND AGES, NOT ALL OF WHICH HAVE BEEN
VERIFIED**

Mutation positive pedigrees [pathogenic, splice site and unclassified]

Aims, once a family has been fully genotyped for the family mutation:

- a) sort out inconsistencies in the pedigree structure
- b) identify obligate carriers, and probable obligate carriers, for research purposes (do not do for unclassified variants)
- c) identify 'sporadic' cancers within the families. Confirm all with Tracey, and perhaps re-test according to guidelines (do not do for unclassified variants)
- d) determine Straddie criteria on completion – need at least two carriers or potential carriers
- e) consider collecting blocks to extend penetrance analyses
- f) send complex issues to KT/GM/JK/JS for review

Mutation negative pedigrees

Aim:

- a) sort out inconsistencies in the pedigree structure
- b) determine Straddie criteria on completion
- c) send complex issues to KT/GM/JK/JS for review

KCONFAB PROTOCOL FOR NOTIFICATION OF SUBJECTS ABOUT GENETIC TEST INFORMATION

Version 5.0

Last Updated	Version	Change
	Notification Protocol GM	
27/11/2002	Notification Protocol v1	
11/12/2002	Notification Protocol v2	Section 3: 8 and 10.
13/12/2002	Notification Protocol v3	Section 3: 4 and 12.
16/06/2003	Notification Protocol v4	Section 12
23/06/2003	Notification Protocol v5	Section 13
16/10/2003	Notification Protocol v6	Section 8

1. Purpose

All clinics with kConFab participants will need to be aware of the following protocol, for families where a variant in a breast cancer susceptibility gene has been identified. This approach aims to:

- a) Provide timely genetic information to participants who have indicated a wish to be informed of progress with genetic testing in their family.
- b) Assure that all clinics associated (now or in the future) with the family deal with a genetic variant in a breast cancer susceptibility gene in a uniform, agreed approach.
- c) Assist the clinics with the provision of information to living affected and at-risk family members.

Subjects have indicated in their consent form whether or not they “wish to be informed if there is a test result that may have implications for myself”.

2. Background

This protocol refers to the way in which kConFab subjects might be informed that a variant in a breast cancer susceptibility gene has been identified in their family and that predictive genetic testing might now be possible.

It should be noted that this might be different from the usual clinic protocol when a genetic variant is identified in a family who are not participating in kConFab. In that case at least one affected member (or obligate carrier) has usually attended a clinic and had blood taken for a mutation search. If the testing identifies a genetic variant in a breast cancer susceptibility gene, then the clinic would usually contact that affected person (or

obligate carrier) first, give the result and assist with identifying the family members who may wish to be informed of genetic test availability. The efficacy of this approach is not known, and may vary from family to family.

In the case of enrolled kConFab families, the family will have been enrolled through one person (affected or unaffected) attending a clinic. Other members may have met with the kConFab nurse in their region either by phone or in person, and a minority of participants may have attended other clinics. The youngest affected participant (or obligate carrier) will usually have been selected by the kConFab clinical investigator as the subject for a mutation search, but that person may or may not have attended a clinic. For kConFab families there are many more people (including spouses) who have been involved in the process, through completion of questionnaires or the giving of blood samples, so more individuals are aware of genetic testing being done for the family. It should be noted that there may be a backlog of families where the mutation has been found prior to now, but where the family has not yet been fully notified, as the family is very large or has been extended further or concatenated by the kConFab research. In that situation, the clinic may not be aware of some at risk family members who require information.

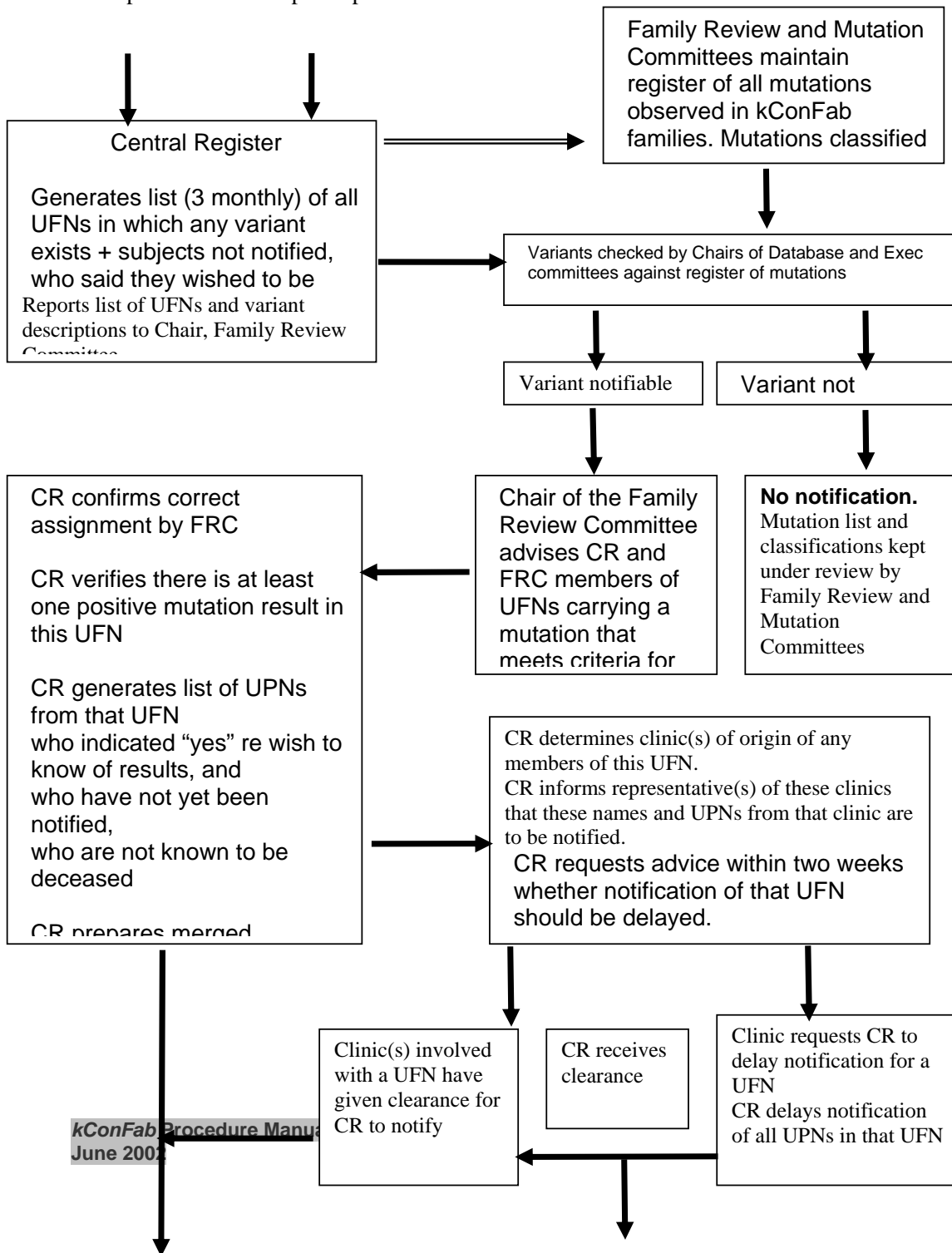
Most participants have indicated that they wish to be informed if there is a (family-related) test result that has implications for them or their family. This is recorded in the kConFab central register. The process below outlines how that information might be provided for kConFab subjects and is summarised in the flow diagram.

3. Protocol

1. A variant in a breast cancer susceptibility gene may be either identified by kConFab, or more often, by a kConFab associated clinical laboratory where one or more of the kConFab family members has attended. Although the mutation searching may have focussed on the youngest affected family member, that person may not necessarily have attended any clinic in person.
2. The variant for the UFN should be notified to the kConFab Central Register through the kConFab administrator (Heather Thorne) if it has not already been entered on enrolment of the family.
3. The Central Register will, every three months, report to the Family Review Committee the UFNs and mutation description of all families in which:
 - 3.1. a breast cancer susceptibility gene variant exists,
 - 3.2. there are family members that wish to be notified, but
 - 3.3. have not yet been notified
4. The central register will verify that the website mutation classification list is up-to-date.

5. A process of auditing mutation reports in the Central Register is in place to verify that positive mutation results have been correctly reported. When these lists are generated a further check will be made to ensure, in families not yet notified, that at least one verified positive result exists in that UFN.
6. The Family Review and Mutation Committees will maintain a list of all variants seen in breast cancer susceptibility genes in kConFab subjects. For the purposes of this notification protocol each variant will be classified as either:
 - 6.1. “Notifiable” - meaning that the variant is likely to increase susceptibility to cancer
 - 6.2. “Not notifiable” – meaning that all available evidence indicates that the variant is a population polymorphism with no significant effect on cancer risk
 - 6.3. “Unclassified” - meaning the evidence has not yet been evaluated
7. These classifications will be updated and added to as new variants are found in kConFab subjects and as the Family Review and Mutation Committees evaluate evidence about them.
8. The chairs of the Database and Executive committees will check which UFNs carry variants classified as “notifiable” and advise the Central Register, copied to the Committee, that notification of those UFNs may proceed. The Central Register will verify against their copy of the list that these are notifiable variants and resolve any discrepancies with the Chair.
9. The kConFab Central Register will then create a notification mail out list, comprising all participating family members belonging to that UFN who:
 - 9.1. have not yet been notified
 - 9.2. have not indicated that they wish for “No Further Contact”.
10. The central register will, when possible, check that list against the death register, to prevent letters being sent to deceased participants.
11. The central register will forward the list of participants to the Clinics where the Research Nurse will record if the participant has consented to notification of genetic test information as noted by citing “Yes” to Q.22 of the kConFab consent form.
12. The clinical service to which subjects may “belong” should have the opportunity to give information first to their patients (before letters to any members of that family go out from kConFab). However many participants will be unknown to any of the clinics. The representative(s) of clinic(s) to which any of the subjects "belong" will therefore be alerted by the Research Nurses about impending notifications. The clinic(s) must indicate in writing (email response acceptable) within two weeks whether notifications to that UFN can proceed or should be delayed. The Central Register can only proceed for a given UFN when given that clearance in writing.

13. The Central Register will then release notification letters to each UFN in a batch, [using the letter attached](#), and providing with the letter a current list of familial cancer services. The Central Registry will inform all of the relevant Family Cancer Clinic heads and the research nurse's when the letters have been posted. Central Registry to remind the RNs to inform the clinic receptionist that they may receive phone calls from participants that have received a notification letter



NOTIFICATION LETTER MARCH 30, 2004.

Date

Dear,

Thank you for your participation in kConFab, the Kathleen Cuninghams Consortium for Research on Familial Cancer. When you joined kConFab, you indicated that you wished to be notified when genetic information became available.

The purpose of this letter is to notify you that our research has identified information relevant to your family. This means that a genetic variation or mutation has been found in your family which may account for the family's experience of cancer. The fact that our research has found this genetic variation or mutation does not necessarily mean that you have inherited this variation.

If you have attended a genetics clinic or a family cancer clinic you may already know whether you have inherited the family's gene mutation. If you have not attended such a clinic and you want to discuss genetic testing with an expert, the procedure is as follows:

1. Contact a family cancer clinic. The address of your nearest clinic can be found on the list provided. Alternatively, you may want to first contact the clinic where your family became enrolled in the study (The XXX clinic, Phone XXXXX)
2. Advise the clinic that you have received a "notification letter" from kConFab and that you would like further information. It will help the clinic if you provide your kConFab Identification Number (.....).
3. The clinic may ask you to obtain a referral letter from your doctor.
4. If you attend an appointment at clinic, the doctor or counsellor will explain kConFab's research findings. They will also explain how you can find out whether you carry the gene mutation that has been found in your family. To prevent any mistakes, the genetic test must be done on a new blood sample which is then tested in an accredited laboratory. When the result of this second test is available, the Family Cancer Clinic will see you again to explain what the result means and to provide guidance and recommendations for you and your doctor.
5. There are usually no costs to you for the clinic attendances or the genetic test.

We strongly recommend that you discuss this letter with a genetic counsellor or doctor at a family cancer clinic. This information may be very important for you or for other family members in reducing the risk of cancer.

We appreciate your continued participation in kConFab. We are keen to ensure that participants in our study receive appropriate explanations, information and counselling about the research results that may be medically significant.

Yours sincerely

(signed)

Chair, kConFab

Attached: List of Familial Cancer Services in Australia with contact numbers

Administration – Project Tasks and Instructions

Recruitment of families

On a monthly basis, the kConFab research nurse's based in the Family Cancer Clinics (FCCs) through out Australia and New Zealand submit pedigree drawings of families have been seen in the local FCC and that may be eligible to recruit into the study.

HT and Judy Kirk review the pedigree drawings and score each family using the following score sheet:

- using the NBCC guidelines - category 1, 2, 3
- Li-Fraumeni – yes/ no
- Number of cases of breast cancer <40
- Number of cases of breast cancer in 40's
- Number of cases of breast cancer in 50's
- Number of cases of breast cancer in 60's
- Number of cases of breast cancer 70+
- Number of cases of ovarian cancer in 40's
- Number of cases of ovarian cancer in 50's
- Number of cases of ovarian cancer in 60's
- Number of cases of ovarian cancer in 70+
- Any with bilateral breast cancer – yes/ no
- Any with breast/ovarian cancer – yes/ no
- Any other cancer – prostate, melanoma, colo-rectal, bowel
- Number of living affected females
- Number if living unaffected females who are first degree relatives of affected (br/ov)
- Number of living unaffected females who are second degree relatives of affected (br/ov)
- DNA collected – yes/ no
- Mutation tested (predictive testing) yes/ no

- Gene type – BRCA1, BRCA2, p53 etc
- Jewish – yes/ no
- Fantastic – yes/ no
- Comments

Families are eligible to be recruited, after the pedigree drawing review by HT and Judy Kirk, if they meet one of the categories (1-3) as listed below in the Noosa Criteria:

Noosa criteria

1. Families in which a predisposing mutation has been identified

kConFab is interested in mutation-positive families where there are two or more carriers (or likely carriers amongst first and second degree relatives from the informative side of the family). Not all mutation-positive families will fit the Noosa criteria.

For inclusion in KconFab, mutation-positive families must fulfil one of the following criteria:

- two living affecteds (i.e. likely mutation carriers)
- one living affected and at least two living first degree unaffected females of a proven or likely mutation carrier
- one living affected and one living first degree unaffected female and at least two living second degree female unaffected relatives of a proven or likely mutation carrier
- one living affected and at least four living second degree unaffected females of a proven or likely mutation carrier
- no living affected but four or more living first degree unaffected female relatives of a proven or likely mutation carrier
- no living affected but three living first degree and at least two living second degree female relatives of a proven or likely mutation carrier
- no living affected but two living first degree and at least four living second degree female relatives of a proven or likely mutation carrier
- no living affected but one living first degree and at least six living second degree female relatives of a proven or likely mutation carrier
- no living affected nor any first degree living female relatives but at least eight living second degree female relatives of a proven or likely mutation carrier.

The criteria for families that have been shown to carry a predisposing mutation are summarised in the following table. Each column in the table shows the

number of affected individuals, and the number of first and second degree female relatives of affecteds that are required for enrolment of a mutation-positive family in KConFab

As of June 2000, until which time the 'Straddie' criteria were used, an exception is made in the case of known BRCA1/2 carriers who are undergoing surgery and wish to give biological specimens to kConFab. In this case the woman can be enrolled in the study even if there are no other carriers, or potential carriers, in the family who wish to be enrolled.

2. Families in which no predisposing mutation has been identified

All of the following are required:

- four or more cases of breast or ovarian cancer (on one side of the family) or two or more cases of breast or ovarian cancer, in same or adjacent generations, if at least one of these cases is 'high risk' (i.e. breast plus ovarian cancer, or onset less than 40 years or bilateral breast cancer)
- two or more living affected
- four or more living first or second degree unaffected female relatives of affected cases

3. HNPCC and Li-Fraumeni Families

- A small number of pedigrees submitted by the FCCs have some features of HNPCC or Li-Fraumeni syndrome. These families are of interest to KConFab because they may carry mutations in genes that are different from BRCA1 and BRCA2 and nevertheless increase the risk of developing breast and ovarian cancer.

After the review HT writes to the kConFab research nurse and clinic head listing which families are eligible to be followed up. For families that aren't eligible, HT describes why they aren't suitable and requests that should the family cancer history change or a mutation identified, the updated pedigree drawing be re submitted for review.

NB. Occasionally a new high-risk category 3 family will present to the clinic appointment that has not been reviewed by kConFab. They participant(s) are keen to donate blood to kConFab on that day. As long as the clinic head and kConFab research nurse is aware of the family history and are confident that the family meets the Noosa criteria, once a consent form is signed, the participant(s) can be bleed. The research nurse's will generate a pedigree drawing with UFN and UPNs and submit the pedigree drawing to HT/JK for review with a tag mentioning that recruitment of this family has already started.

In-the-field the research nurse's are occasional informed about the cancer history of a family member that isn't eligible to be recruited under our guidelines (usually a second degree relative), but appears to be of interest. The research nurse informs HT about this family member and discusses if they should be recruited.

HT will always refer back to JK, GCT or JS if there is any doubt about whether is this family member should or shouldn't be recruited.

Every 6 months, GCT requests from central registry a listing of families that have been downloaded. HT cross checks the UFN to the original clinic pedigree drawing number and notes how the family was recruited into kConFab. The code used for this listing is:

- 1 = Families in which no predisposing mutation has been identified
- 2 = Families in which a predisposing mutation has been identified
- 3 = HNPCC and Li-Fraumeni Families
- 4 = BRCA1/ 2 carriers who are undergoing surgery and wish to give biological specimens to kConFab. In this case the woman can be enrolled in the study even if there are no other carriers, or potential carriers, in the family who wish to be enrolled.

The coding above needs to be linked to the UFN at the central registry database so that researchers know how the family was accepted into the study.

The RNs pass the UFNs onto HT as soon as they are issued.

HT will link the UFN to the clinic ID number on the family review work/score sheet. This will be useful when auditing and scoring how families were accepted into the study

Approach letters

The following are copies of the approach letters that the kConFab research nurses use when contacting the participants and various treating doctors, pathology and medical records departments. Please note there may be a small variation in the letters used between site to site due to the wishes of the local clinic heads.

Approach letter for FCC patients KConFab/Clinic Letterhead

Dear

I am writing to you as a follow-up to your consultation here at the Familial Cancer Clinic, to invite you to participate in a new national research study. The Kathleen Cuninghame Foundation National Consortium for Research on Familial Breast Cancer (known as KConFab) has been formed to answer important questions regarding the familial aspects of breast cancer. In particular, in this study, we want to find out:

- how often faults (mutations) in breast cancer genes occur in the Australian population;
- the kinds of genetic faults which predispose Australian families to breast and ovarian cancer;
- the risk of cancer, the type of cancer and the age of onset of cancers which are associated with each gene and each kind of fault;
- what lifestyle and environmental factors influence the risk of developing cancer in people who inherit these mutations and which of these factors delay or accelerate the onset of cancer.

The individuals who can best help us answer these questions are men and women, both with and without cancer, from families where there has been a history of breast or ovarian cancer, usually in a number of individuals over several generations of the family.

We are inviting a number of families who have attended the Clinic to participate in this study. Some of these families have already had genetic testing and have obtained results, some are waiting on results and some have not yet decided to proceed with genetic testing. Participation in this research study provides the opportunity for a more complete gene mutation search (genetic test) than is generally available through the Familial Cancer Clinics however, we can not guarantee that we will be able to conduct all tests on all samples. Individuals may choose whether or not they wish to know the results of genetic tests.

A member of our research team will be contacting you soon to give you further information about the study and to offer you the opportunity to participate.

Participation is completely voluntary. If you prefer at this stage not to be contacted, or if you have questions, please phone either myself or our Genetic Counsellor on

While we cannot promise that you will benefit from being a participant, we do hope and expect that the outcomes of the research made possible by this study will be of benefit to members of families like your own.

Yours sincerely

.....

Approach letter for relatives of FCC patients

KConFab/Clinic Letterhead

Dear (Relative's Name)

I am contacting you because I am already involved in a national research study and the researchers would like to send you some information, allowing you a choice as to whether to participate. Individuals who join the study are asked to answer questions concerning their medical history, health and lifestyle. In addition they would like to take a small sample of blood (20ml) for research.

You are invited to take part in a new national breast cancer research study. The Kathleen Cuninghame Foundation National Consortium for Research on Familial Breast Cancer (known as KConFab) has been formed to answer important questions regarding the familial aspects of breast cancer. In particular, in this study, the researchers want to find out:

- how often faults (mutations) in breast cancer genes occur in the Australian population;
- the kinds of genetic faults which predispose Australian families to breast and ovarian cancer;
- the risk of cancer, the type of cancer and the age of onset of cancers which are associated with each gene and each kind of fault;
- what lifestyle and environmental factors influence the risk of developing cancer in people who inherit these mutations and which of these factors delay or accelerate the onset of cancer.

The individuals who can best help us answer these questions are men and women, both with and without cancer, from families where there has been a history of breast or ovarian cancer, usually in a number of individuals over several generations of the family.

A number of families are already involved in this study. Some of these families have already had genetic testing and have obtained results, some are waiting on results and some have not yet decided to proceed with genetic testing. Participation in this research study provides the opportunity for a more complete gene mutation search (genetic test) than is generally available through the Familial Cancer Clinics. Individuals may choose whether or not they wish to know the results of genetic tests.

A member of the research team will be contacting you soon to give you further information about the study and to offer you the opportunity to participate. Participation is completely voluntary. If you prefer at this stage not to be contacted, or if you have questions, please phone a member of the research team on

Alternatively, you may wish to return the accompanying form to indicate your willingness, or otherwise, to participate and send it back in the stamped, addressed envelope provided. If you indicate that you do not wish to take part, no further action will be taken. However, if we do not hear from you over the next few weeks, a member of the research team who interviewed me....., will get in touch with you to give you the details of the research, answer any questions you may have, and to obtain your consent to join the study.

While the researchers cannot promise that you will benefit from being a participant, they do hope and expect that the outcomes of the research made possible by this study will be of benefit to members of families like our own.

Yours sincerely

(Family members name)

**Response Letter from Relative
KConFab/Clinic Letterhead**

Research Project: The Kathleen Cuninghame Foundation National Consortium for Research on Familial Breast Cancer (KConFab).

Chief Investigators: Professor Joseph Sambrook, (Insert Local Investigator Names)

NAME: (Mr. Mrs. Miss Ms.).....

ADDRESS:
.....
.....

TELEPHONE:
(Home) (Business)

Please tick the appropriate response and return in the pre-paid envelope.

.....I agree to be contacted about the breast cancer family study.
I would like to know more about the study

.....I do not wish to be involved in the breast cancer family study.

COMMENTS:
.....
.....
.....

Signature: Date:

Thank you for your assistance.

KConFab/Clinic Letterhead

Dear Dr.....

RE:.....

DOB:..... Deceased Date:.....

The deceased was the relative of a participant in our study, The Kathleen Cuninghnam Foundation National Consortium for Research on Familial Breast Cancer. As part of the study we are trying to verify all reported cancers in the family.

(Name of study subject) believes that their relative received treatment for breast cancer in your hospital in (date), and has consented to allow us to access information on (name of deceased); see attached consent form.

I would be grateful if you could supply us with any information about (name of deceased)'s medical condition when they received treatment at your hospital. In particular, copies of pathology and/or autopsy reports would be most helpful.

A self addressed envelope is enclosed.

Please contact me or any of my staff on.....if you have any questions about this request.

Thank you for your assistance in this matter.

Yours sincerely

KConFab/Clinic Letterhead

Dear.....

We would like to thank you for your participation in our study of familial breast cancer.

At the time of your interview you indicated that you would be willing to give a blood sample of 20mls to help us in our research.

Since speaking with you we have contacted the doctor you nominated, (Dr.....), who is willing to take your blood sample and is expecting you to present within the next three weeks. Please make your appointment on a Monday, Tuesday or Wednesday so that the blood can reach our laboratory for us to process it before the week end.

We very much appreciate your cooperation. If you have any queries please do not hesitate to contact me or a member of the research team on

Yours sincerely

“Soft” Introduction letter

kConFab/Clinic Letterhead

Dear

Thank you for participating in this study. I have enclosed a research information sheet, for you to keep, so that you can understand the background and purpose of the research.

In addition, there are two copies of the research consent form. The consent form is rather lengthy, but I will be phoning you to discuss any questions or concerns you have. Please take the time to read all of this information about the study. After my phone call, I would like you to sign one copy of the consent form and return it to me in the reply paid envelope. You may keep the other forms for your own information.

As mentioned on the consent form and in the research information sheet, we require from all individuals involved in the research project:

- a signed consent form.
- an updated family history.
- questionnaires filled in about your health, life style and diet.
- donation of a small sample of blood.

It is possible that testing of this sample may indicate the presence of a faulty gene. Faults in certain genes may result in an increased risk of breast and other cancers. We wish to determine how frequently these faults occur in breast cancer patients and their families within the Australian population.

All individuals involved in the study will receive a yearly newsletter outlining the progress being made. Once again, we would like to thank you for your involvement in this important national study. If at any stage you should have any questions about the project, do not hesitate to contact a member of the research team.

Yours sincerely

.....
Research Nurse

Completed families – thank you letter

Below is a thank you letter that can be sent to the Family Contact person and/or co operative family member(s) once a family is completed.

The letter can be placed in a Beryl Martin designed card.

HT supplies Beryl Martin cards and envelopes to the research nurse's.

On behalf of our entire research team, we would like to thank you and your family for your valuable contribution to breast cancer research carried out by the Kathleen Cuninghame Foundation Consortium for Research on Familial Breast Cancer (kConFab).

An important aim of our research is to find out why some families have a history of breast cancer and some do not. To find the answer to this and other questions, we need to collect data on the lifestyle of over 700 families; and we need to analyse blood samples from more than 7,000 women and their relatives. This is a large task that will take us three years to accomplish. So far, we have collected blood samples and epidemiological data from approximately XXXX women and we have identified over XXX families with a significant history of breast cancer. We are grateful for the time that people like you have so generously given to this study of breast cancer in Australian families. We hope that the answers we obtain at the end of the study will bring benefit to all women who are at high risk of developing the disease.

kConFab is a national consortium of some XX researchers and clinicians from 5 States in Australia who are working as a team on this project. We are grateful to the Kathleen Cuninghame Foundation and the Federal and State Governments for grants and other support for this work.

There is a possibility that we may need to contact you again in the future. Therefore, if you should move, we would appreciate knowing your new address.

With best wishes,

kConFab research nurse who has recruited the family

Consent and Research information sheets

These forms are given to potential participants who mention to the research nurse or Family Cancer Clinic staff that they are interested in finding out more about the study and would possibly like to be involved.

To use these forms at each site, above the kConFab logo on the front page place:

- the local institutions logo and local investigators

On both forms add:

- the local research nurse(s) name and contact details
- full details of the local ethics chairperson or complaints officer contact should there be a complaint
- HT's name and contact details should they require further information about the project
- These forms are available at www.kconfab.org

Budget

HT receives a budget account each month from the PMCI research business manager, which details all money that has paid in and out of the kConFab account. The finance department at PMCI has audited the account received. The budget is reviewed each month to isolate any irregularities. The kConFab budget is presented twice yearly to the executive committee for review and approval. Prior to the budget being presented to the executive committee, HT will hold discussions with the executive director to confirm the priorities of the consortium and where money should be spent. Budgets are worked around the priorities stated

Executive and sub committee meetings

Two executive and one sub committee meeting are held through out the year. Some sub committees will meet more than once depending on the issue that needs addressing. HT will organise venue, airline tickets and assist executive director with the venue. Try and give everyone enough warning about these meetings – especially the clinicians as they have clinics booked 6 months in advance. Annual reports from sub committees and research projects need to be included in folders for the meetings. The deadline for sub committee reports and research project reports is 2 weeks before an executive committee meeting. Make sure that every one is aware of this deadline.

Annual Reports

Note that annual reports are required to all granting agencies and sites where ethics approval has been gained. Note in diary due by dates.

Forms to be used are available from each agency and local ethics committee

Research nurse meetings

A one day annual meeting is held involving all of the core kConFab research nurse's, database staff and managers from the kConFab Clinical Follow up project and Psychosocial team. kConFab pays for airfares and living expenses fore the core research nurses and database manager to attending the meeting. The other kConFab groups pay for themselves out of their own budgets.

Transfer of Materials Agreement

Below is a copy of the MTA that is currently being used. This MTA must be signed by the head of PMCI research, Dr David Bowtell and the appropriate investigators/head of department who are receiving the kConFab material before any material is sent. A copy of all signed documents are kept with the kConFab executive director and manager.

TRANSFER of Materials Agreement

This Agreement is made on the day of

BETWEEN

Peter MacCallum Cancer Institute, a metropolitan health service incorporated in accordance with the *Health Services Act* (1988) of St Andrews Place, East Melbourne, in the State of Victoria, Australia ("PMCI")

AND

("Institution")

"Recipient".

background

A The Kathleen Cunningham Foundation National Consortium for Research on Familial Breast Cancer ("kConFab") co-ordinates a study on mutations in known breast cancer predisposition genes. In the course of the study, members of kConFab collect clinical details and blood and tissue samples from men and women from potentially high-risk families.

B PMCI distributes the clinical data and the samples of genetic material, blood cells and tissue samples collected by kConFab.

C PMCI has agreed to make available to the Recipient some or all of the clinical details and / or samples of genetic material, blood cells and tissue samples for the purpose of allowing the Recipient to evaluate and use the material in the course of XXX's research on the terms set out in this Agreement.

AGREEMENT

For the purposes of this Agreement, the "Material" means DNA and modifications or derivatives developed or discovered by the Researcher in the course of the Research. If the Recipient makes an invention, discovery or any other intellectual property right that is derived or generated by him as a result of his use of the Material he will promptly inform PMCI. Inventorship shall be determined in accordance with Australian Law (if patentable) or by mutual agreement of the parties (if not patentable) and taking into account the respective roles and contributions of the parties to the production of that invention, discovery or intellectual property right. In the case of a joint invention, the parties agree to negotiate an agreement which shall provide, inter alia, for the sharing of income,

patent costs and the administration of any patent in the various countries in which it is filed.

PMCI grants the Recipient a non-exclusive licence to use the Material for the purpose of identifying mutations in the *ATM* gene (the "Research"), in consideration for which the Recipient agrees to be bound by this Agreement.ⁱ

The Recipient must not use the Materials for any profit making or commercial purpose, unless the parties have executed a written agreement for the profit-making or commercial use of the Material. PMCI does not grant any right to an agreement for the commercialisation of the Material in this Agreement.

The Researcher must:
not use any genetic material, blood cells or tissue samples provided by PMCI in human beingsⁱⁱ; and
comply with all relevant laws and Standards in relation to the use of the Material.

The Recipient must not:
transfer, sell or otherwise distribute Material; or
assign its rights under this Agreement.

If the Materials supplied are used in research that generates, or from which is derived, any invention (whether patentable or not), or any commercially valuable property or know how that could not have been discovered without the use of the Material, the Institution will inform PMCI and will negotiate in good faith with PMCI any intellectual property rights to that invention, property or know how as the case may be, taking into account the value of the parties' respective contributions to same in addition to Australian Law relating to inventorship.

The Recipient must not disclose the Material to any person other than where:
The disclosure is required by law;
The disclosure is made to those of the Institution's researchers who are directly involved in the Research and who are placed under an obligation to observe the terms of this Agreement; or
PMCI consents in writing to the disclosure.

To the extent permitted by law, PMCI excludes warranties of merchantability, fitness for a particular purpose and any other warranties, express or implied. PMCI makes no representation and provides no warranty that the use of the materials will not infringe any third party intellectual property rights.

PMCI shall not be liable for any loss, claim, damage or liability (except as caused by the negligence of PMCI) that may be incurred, accrued or otherwise undertaken by the Recipient and the Institution in his or its performance of this Agreement and NCI, as an agency of the United States, assumes all and any

liability that may arise under this Agreement to the extent provided under the Federal Tort Claims Act (28 U.S.C. §171).

The Institution must obtain and maintain adequate insurance in respect of its use of the Material.

The Institution must inform PMCI in writing of results of the Research that are directly related to the Material or that could not have been discovered without the use of the Material, as soon as reasonably practicable, but no later than 60 days from the results becoming first available to the Recipient.

On conclusion of the Research, the Recipient must, at its own cost, return or dispose of all remaining Materials or any copies made of the Material, as instructed by PMCI. The Recipient must supply PMCI with any reports prepared and details of any discoveries, results or comments made in relation to the Research within sixty (60) days of the conclusion date of this Agreement.

This Agreement shall be construed, governed, interpreted and applied in accordance with the laws of the State of Victoria, Australia and the parties agree to submit to the jurisdiction of the courts of Victoria and the Commonwealth of Australia in respect of all matters and things arising out of this Agreement.

This Agreement can only be varied by the parties in writing.

Clauses 6, 7, 8 and 9 survive termination of this Agreement.

Signed for and on behalf of The Peter MacCallum Cancer Institute by:

.....
(Name)

.....
(Title)

.....
(Date)

Signed for and on behalf of

Signed by

.....
(Institution)

.....
(Researcher)

.....
(Name)

.....
(Name)

.....
(Title)

.....
(Title)

.....
(Date)

.....
(Date)

Scientific meetings:

kConFab holds a biannual scientific and clinical meeting. Sponsorship is obtained from companies to try and minimize money being spent from the core research grant. The organising committee needs to develop a programme and estimate a budget 12 months in advance so that companies have time to access the proposal from kConFab,

Grant payments:

Tax invoices to be generated 2 weeks before each quarter and sent to the agencies that supply project funding:
Cancer Councils, NHMRC, NBCF

Wages:

Contact business managers at each site and request tax invoices from Family Cancer Clinics and laboratories 1 month before the beginning of a quarter so that wages can be paid.

kConFab Appointments:

A letter must be sent to head of department confirming that all appointments made by kConFab will be honoured for a determined period as determined. If the appointment to be made is based at PMCI, obtain approval from the CEO before advertising for the position. Job description and advertising description must be completed before job can be advertised at PMCI. Formats are available from the PMCI research secretaries

Payment to clinical laboratories for mutation test results:

Review every 6 months mutation test results supplied by clinical testing laboratories. kConFab will pay \$300 per test result (positive and negative) per family to the testing laboratory. Payment will only be made to one laboratory for each family. Usually the laboratory that is first to provide the mutation test result to kConFab will be paid. Occasionally one off payment schemes for genetic testing are available. Please refer to the chair of the biospecimen committee for clarification of these one off schemes.

Purchase of computers and software:

kConFab purchases all computers, printers, software and pays for upgrades and repairs for all the kConFab computers used in the Family Cancer Clinics and database department. It is important before any computers are purchased that HT and the Family Cancer Clinic department head speak to the IT department where the computer will be located to ensure that the IT department are happy to support the kConFab computer and organise the connection and back up facilities required. KConFab is flexible in how the equipment is purchased. HT can order and pay for the equipment once the local IT head provides full computer/software specification details, or, the local department can order and pay for the equipment and send the invoice to HT for reimbursement.

Applications to the Cancer Registry for Cancer Verifications

Down load application form and guidelines from each states home page. When approval received from each state lodge approvals to:

Edith Christensen

Health Registers and Cancer Monitoring Unit

Australian Institute of Health and Welfare
GPO Box 570 Canberra ACT 2601
Ph: +61 2 6244 1063
Fax +61 2 6244 1044
E-mail: edith.christensen@aihw.gov.au
www.aihw.gov.au

AIHW – National Death Index

Mr John Harding
Head, Health Registers and Cancer Monitoring Unit
Australian Institute of Health and Welfare
GPO Box 570 Canberra ACT 2601
Tel: 02 6244 1140
Fax: 02 6244 1044

* South Australia needs to be approached and dealt with directly

Ms Juanita Lacar
Human Research Ethics Sub-Committee
Research and Evaluation Branch
Department of Human Services
P O Box 287
Rundle Mall
Adelaide, 5000

Home page

The kConFab home page can be found at :

www.kconfab.org

For updates to the home page, HT and/ or GCT supply Rohan Farrell, the IT head at PMCI, the word or excel documents to be used.

Email: Rohan Farrell <r.farrell@pmci.unimelb.edu.au>

Communicating with the community representative

kConFabs community representative is:

Mrs Gerda Evans

Email: gerda@bigpond.net.au (Work)

The community representative is an essential member to any group like kConFab. They are able to bring to the executive committee and general membership a wider perspective and understanding on issue related to the disease. Their own personal outcomes, and that of others they know in special interest community groups, from dealing with health professionals are an important aid in delivering improved service, health and educational information. Issues of ethics and appropriate delivery of research findings has also been an area where the kConFab community representative has had a major input. . The community representative is also an invaluable link to other "like"

associations and community groups. Through them the network for distributing updated research results and educational information is enhanced.

Links to other breast cancer organizations

National Breast Cancer Foundation
Level 4, Suite 402
90 Pitt Street Sydney 2000
Ph 02 9235 3444
Email: NBCFoundation@aol.com

Breast Cancer Network Australia
PO Box 4082
AUBURN SOUTH VIC 3122
Ph: (03) 9805 2500
Email: beacon@bcna.org.au

National Breast Cancer Centre
Locked Bag 16 Camperdown
NSW 1450 Australia
Ph: 02 9036 3030
Email: director@nbcc.org.au

Links to other Research Projects

Haplotyping Analysis:

Kelly Ewen-White, PhD
Manager, Genotyping Section, Australian Genome Research Facility
Walter & Eliza Hall Institute of Medical Research
Royal Melbourne Hospital 3050, Victoria,
Ph: +61 3 9345 2669
Fax: +61 3 9345 2678
e-mail: ewen@wehi.edu.au

Australian Breast Cancer Family Study (ABCFS)

Ms Judy Maskiell
The University of Melbourne
723 Swanston Street Carlton, 3053
Phone 03 8344 0694
Email: j.maskiell@gpph.unimelb.edu.au

Teleconferences – ring 1800 011 080 to make a booking. Take note of the dial in and pin number to be used

Donations:

For the general public and kConFab participants that ring wanting to donate funds to kConFab, send them a kConFab newsletter and refer onto Ms Sue Murray at the NBCF – to those seeking general information supply telephone and email contact details.

Ms Sue Murray:

90 Pitt Street Sydney 2000

Ph 02 9235 3444

Email NBCFoundation2@aol.com

On receipt of money, send a thank you letter to the individual/group that did the fund raising

Newsletter

An annual newsletter is printed. Start preparing stories for the newsletter 6 months in advance. Contact all kConFab members and ask for ideas that they think may be of interest to publish. Also highlight recent kConFab research studies and list full details of FCC contacts.

The yearly newsletter post out may be a good time to alert participants about informing kConFab about any change of addresses.

Before the mail out, supply Australia Post on a disc with the names and addresses of kConFab participants currently held on the database so that a cross check can be made and addresses updated and corrected.

Australia Post contact:

Mr Alan Lawrance

C/O COA Processing Coordinator

Level 4 123 Lonsdale St

MELBOURNE VIC 3000

Email: alan.lawrance@Geospend.com.au

When the address file is returned from Australia Post, please check:

- that the updated address is more current than the address kConFab holds.
- Australia post provides the date that the address was updated.

The following form can be inserted in the envelope with the newsletter and a reply paid envelope addressed back to:

kConFab

Research Department

Peter MacCallum Cancer Institute

East Melbourne, 3002.

Please refer to **Printer** page 61 as they can organise the printing of this form and reply paid envelope along with the newsletter:

Has Anyone In Your Family Changed Their Address?

We are aware that many of the addresses we have for people in kConFab are now out of date.

This makes it impossible to contact people with newsletters or when we have important information for them.

If anyone in your family has changed their address in the past 3 years, please complete the section on the back of this form.

Your Full Name:

Your Date of Birth:.....

Please list below the full name and date of birth of any family members who have changed their address since enrolling in kConFab.

Person 1:

Full name: _____ Date of Birth: / /

Previous address: _____

New address: _____

New telephone numbers: Daytime: _____ After hours: _____

Person 2:

Full name: _____ Date of Birth: / /

Previous address: _____

New address: _____

New telephone numbers: Daytime: _____ After hours: _____

Person 3:

Full name: _____ Date of Birth: / /

Previous address:

New address:

New telephone numbers: Daytime: _____ After hours: _____

Person 4:

Full name: _____ Date of Birth: / /

Previous address:

New address:

New telephone numbers: Daytime: _____ After hours: _____

Need more space? Please attach details on an additional sheet of paper

**Please return completed form to:
kConFab, Research department
Locked Bag 1, A'Beckett Street
Melbourne VIC 8006**

All change of address forms sent back to kConFab are updated at the central registry and the forms are also sent back to the relevant clinic so that the updates can be made on the local clinic FBI database.

Graphic Artist – kConFab newsletter

Ms Maggie Lenaghan
Media Relations and Publications Coordinator
Centre for Genetic Epidemiology

Department of Public Health
The University of Melbourne,
723 Swanston Street, Carlton, Victoria, Australia 3053
Phone: 3 8344 4540
Email m.lenaghan@unimelb.edu.au

Australia Post – Pre Printed Envelopes:

Application forms available from Australian post offices (red forms) fax application to Australia post on 03 8626 1895. Fax completed form to 03 8626 1895. Pass art work onto approved printer (see Neil Maynard under General Business)

Printer

Neil Maynard
Interprint Digital.
Phone 03 9555 363361
Fax 03 9553 3052.
Email: neil@interprint.com.au

Printer - Epidemiological Questionnaires

NCS Australia
Tel: 03 9873 8800
Fax: 03 9873 8950
Female questionnaires ref # 8634
Female proxy questionnaire ref # 8636
Male questionnaire ref # 8637
Male proxy questionnaires ref# 8635
kConFab Dietary questionnaire ref # 8517

Computer Items

Progeny customer number
0001 502 572

Laboratory Items:

Printer for biospecimen labels:

Brother PT-1100 printer

Labels for biospecimen tubes:

Brother TZ 231 12 mm laminated white label for the PT-1100 printer

Available from Officeworks or other major office suppliers

HT orders at discount price from

Australian Business Machines

506 Queensberry Street, North Melbourne

Ph 03 9328 2503

Fax 03 9328 2701

Preferred Laboratory Suppliers

Many chemicals and plastic wares are available through the PMCI supermarket.

The following is a list of items not held by the PMCI supermarket and that need to be ordered externally via a PMCI research F18.

Fetal Calf Serum

Present batch number 607 1720, Cat #15010 -0500V

Trace

Bio bottles

Catalogue # B/ 2.5

Bio bottle outer cartons

Catalogue # BC/2.5

Marair.

Tel 03 9335 2699

Small bio bottle

Shipper infectious substance

Cat#LBSLABPAK11

Labtek

tel: 07 3881 1388

Ficol Paque research grade

catalogue # 17-1440-02

Pharmacia-Biotech

Cryocolour colour coded tops (100 coloured inserts per box)

Mauve catalogue # 3-75922

Pink catalogue # 3-75884

Grey catalogue # 3-75906

*White inserts are free with freezing vials

Medos

TRIS - EDTA

X100 conc

Sigma

DMSO

Catalogue # 10323.4L
BDH

Vacurette 9 mls EDTA tubes (1200 per box)
Greiner

ACD tubes
Cat "455055
Interpath 50/tray \$14

Cardboard white boxes for vial storage
Catalogue #B2C
Plus 81 cell divider
Catalogue # D81 per packet of 10
Astral Scientific

RNA/ater
Cat# 7021
Ambion

To make Guthrie cards
Cotton paper can be purchased from Schleicher & Schull
Catalogue # SS32218, 580x590 100 sheets per box
Medos
Have cotton paper delivered to Embassy Press for printing and cutting
Template of Guthrie card held at Embassy Press
Director, Mr John Isreal
45 Rushdale Street
Knoxfield, 3180
Tel 03 9764 9188

Transportation:

Consignment Notes:

Blue Circle Overnight deliveries:

Overnight consignment notes to be ordered as requested.

Below are the 3 types of consignment notes ordered from blue circle:

I wish to purchase **XXX** consignment notes pre paid /3kg in total

100 notes

BLANK

BLANK

100 notes

From

BLANK

To

Heather Thorne
Research Dept, 2nd Floor
Peter MacCallum Cancer
Institute,
East Melbourne, 3002

100 notes

From

kConFab nurse
Familial Cancer Clinic
Westmead Hospital
Westmead, 2145

To

Blank

Please add on all the printed notes, "IATA, 650 approved"
Please refer to our account number XXX for billing.

Fax order to Peter Morley on 03 369 6800

Plastic gov bags can also be added to the order and are free

When booking quote account # MP114 and the kConFab cost centre 30098

Blue Circle – Dried Ice Deliveries:

For pick up of esky's in all Australian Capital cities with fresh tissue to be delivered to Heather at PMCC contact:

Mr Blair Cullen Phone 03 9258 6042

- Inform Blue Circle that the esky contains dried ice
- write UN1845 on the consignment note
- place black and white dangerous sticker on the outside of the esky
- fill in over night consignment notes supplied

SkyNet – Overnight deliveries from New Zealand

To order 1kg consignment notes for New Zealand ring:

Gerard Rotse or Morag with problems

Tel: 03 9329 7377

Tel: 02 9693 5575

Fax 03 9329 1926

Or

Morag for complaints and tracking advise

When ordering consignment notes request “Blood non infectious – IATA 650 approved” be pre – printed on the consignment notes.

Alert Auckland research nurse that along with the consignment note, New Zealand customs declaration form must also be attached to the bio bottle. HT has copies

For advise to import blood from New Zealand to Australia contact:

Shelley Gross 03 9246 6756 (Head of Department Dennis Way)

With delays at customs Sydney contact Clare McKee

Tel:02 9364 7300

email: claire.mckee@aqis.gov.au, or

Mario Benet

Tel: 02 9364 7210

Customs agent being used by Skynet are:

Century Customs (NSW)

Also contact Mathew at Century Customs if there are delays in getting shipment through Sydney customs:

matthewa@century.tradeway.com.au

Tel: 02 9700 7238

To send empty bio bottle back to the Auckland clinic, ring Gerard at Skynet and obtain either a 10kg shipping box @ \$85, or 25kg shipping box @ \$125 with appropriate consignment note. Fill box up with bio bottle, newsletters pre printed envelopes.

*** Don't forget to attach Australian customs clearance declaration form – HT has copies**

Deleted: ⁱ kConFab may wish to charge a fee for the transfer of materials, such as an administrative fee to recover the costs of reviewing the research proposal and request for the materials and of providing the materials to the Recipient. An amendment can be made to clause 2 to give the option of charging a fee. The Agreement as currently drafted provides for the recovery of any GST that must be made by PMCI / kConFab for the provision of the materials to the Recipient as a result of the charging of a fee. (See note (iv), below.)

Deleted: ⁱⁱ Is this phrase wide enough for kConFab's purposes or should it also refer to use in human body fluids, extracts of human tissues, human tissue in explant culture or human cells in cell culture?