

INSTRUCTIONS FOR PATIENT RECRUITMENT AND COLLECTION OF BIOLOGICAL SPECIMENS

FOR KCONFAB FAMILY CANCER CLINIC NURSES

APRIL 2005

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 because they fulfil the eligibility criteria.

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-filed 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 these procedures 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. 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.

BLOOD

1. 20 ml blood in EDTA to be collected for KConFab from every consenting and relevant adult (>18 years) member of the families requested by KConFab.

This means

- a. All alive affected (with breast or ovarian cancer).
- b. All first degree relatives of any affected.
- c. All relatives (including spouses) who connect affected, even if not first degree.
- d. **All first degree relatives of BRCA1/2 carriers where ethically possible.** We realise that in many cases this is not possible because the RNs do not know which members of the family are carriers. Therefore this can only be done if the carrier tells the RN of their carrier status, or if the Family Cancer Clinic informs that RN that the mutation results have been received and that the RN can now approach their first degree relatives.

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 ml 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 Centre 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). Pathology companies willing to do these 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 (pro forma 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, the 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 pro forma 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 (heather.thorne@petermac.org) and phone/fax of all samples that are shipped, including their numbers, names and date of birth.
4. Blue Circle is the official carrier of the biological specimens. Once a blood sample(s) are collected,
 - a. 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.

- b. On the outside of the cardboard box place a pre-paid consignment note (make sure senders section is filled in) addressed to Heather Thorne, Peter MacCallum Cancer Centre.
 - c. Ring Blue Circle on 1300 30 76 30, and inform them of where the sample is to be collected from.
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, mouth washes are a poor alternative. Contact Heather Thorne for details.

ARCHIVAL PATHOLOGICAL MATERIAL

Initially, pathology reports and paraffin blocks 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.

1. Informed consent will be obtained for access to this material from the patient, or next of kin if the patient is deceased.
2. 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.
3. 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 ml 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:

1. Seek permission from the relevant surgeon and determine which pathologist will be used. Send the pro forma letter to surgeon with details of pathologist etc and questions re menstrual cycle to be filled in on day of surgery.

2. 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.
3. Notify Heather Thorne of the patient's and surgeon's details.
4. Send copy of the consent form to Heather.
5. Inform the designated pathologist of the patient's name and date of surgery. Discuss the protocol for processing the specimen with them and send them a copy if they wish. Warn them that the RN will be bringing the sample to them from surgery (on wet ice).
6. 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.
7. 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.
8. 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.
 - a. **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.
 - b. 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.
9. 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.
10. On the day of shipment from all sites within Australia, ring Blair at Blue Circle Melbourne on 1300 30 76 30 and book the shipment – mention that it is a dry ice shipment. Request that collection of dried ice shipment be mid afternoon at your site and delivered by noon at the Peter MacCallum Cancer Centre the following day. Use Blue Circle next-day delivery consignment notes as supplied and addressed to:

Heather Thorne
2nd level, Research Department
Peter MacCallum Cancer Centre,

East Melbourne, 3002

11. Label the con note as follows:

- Heather's phone number at the PeterMac (03 9656 1542)
- 'Dried Ice UN1845' under the description of goods
- Blue Circle will place the miscellaneous dangerous goods note onto the esky

Make a record of the consignment number,

12. Notify **Heather** (by phone and email with copies to Lynda and Dani in case she is away) and the consignment number.

13. Blue Circle will confirm with you the next day what time the esky was delivered at PeterMac and who signed for the esky.

14. 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 PeterMac, place an ice pack into the bio bottle.

15. 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.

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. 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.

- Central registry may decide to merge the 2 families into 1 family. The RNs will be advised by the central registry on how this is to be done.
- Place other UFNs or clinic number on pedigree drawings submitted to the central registry and HT