Ethically Defensible Plan

TR-ANZGOG

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Scope

This Ethically Defensible Plan (EDP) has been developed in accordance with the *National Statement on Ethical Conduct in Human Research* 2007 (Updated 2018) The National Health and Medical Research Council, the Australian Research Council and Universities Australia. Commonwealth of Australia, Canberra, and with reference to *Guidance for a Ethically Defensible Plan, NSW Health Statewide Biobank* 2018, NSW Ministry of Health, North Sydney.

Plan

In the event that an incidental or research finding is made while undertaking research utilising biospecimens and/or data from TR-ANZGOG that may have an implication for a participant or their family, the Investigators have developed an EDP, in accordance with the recommendations of the *NHMRC National Statement on Ethical Conduct in Human Research* 2007 (Updated 2018).

TR-ANZGOG will begin with the formation of an EDP Panel willing to provide their expert opinion regarding the specific situation. This group is likely to include:

1. Representatives from the TR-ANZGOG Steering Committee
2. ANZGOG Chair, or appropriate oncology delegate
3. Director of a Familial Cancer Clinic (FCC)
4. An expert in the field of research under review
5. Others as deemed appropriate considering the specific situation under review

The group will discuss the situation brought to the attention of the TR-ANZGOG investigators, discuss the matter and plan a course of action.

The implementation of the EDP will include the following:

1. Confirmation that the research finding eg a germline mutation, is pathogenic and/or actionable, eg, in published literature the mutation is linked to the development of disease.
2. The EDP protocol will then depend on the survival status of the patient.
3. If the participant is alive, they will be contacted by their primary treating physician, and invited to attend an appointment at the site where the participant originally consented to their sample being used in research (if possible).
4. At this meeting the patient may see either or both the primary treating specialist physician and a genetic specialist and given counselling as per usual care.
5. The specialist will inform the patient that a research finding has been reported which might have a health implication for them or their family.
6. It will be advised to test a new blood sample since the research finding is not a clinically validated result.
7. If the patient elects to undergo genetic testing, a new blood sample will be taken and tested in an accredited clinical testing facility.

8. The patient will be informed of the testing result using the usual clinical protocols, ie if results of the clinical testing are significant and may have a health implication for the patient/or family member, then the patient will be offered clinical care if necessary and genetic testing/counselling for family members.

If the patient is known to be deceased, then it is not possible to acquire a new independent blood sample to test.

TR-ANZGOG will routinely store blood samples in aliquots. In this case a new aliquot of blood will be taken from biospecimens storage, the DNA extracted and sent for testing in an accredited clinical testing facility.

If results of the clinical testing confirm the research finding and have a health implication for the family members, then the next of kin that has been nominated by the participant will contacted by the genetic counselling service and offered counselling/genetic testing for family members.

Points to consider:

- TR-ANZGOG itself is not likely to be performing research that will yield research results; rather it will be providing biospecimens and data to researchers who will perform the testing. Therefore, the researchers who apply for material will need to be aware of TR-ANZGOG's position regarding this EDP. The EDP will be submitted to the HREC for approval and the approved plan will be made available to research applicants.
- The research results are produced in a research laboratory environment and not necessarily in a NATA accredited testing laboratory. Therefore research results cannot be relied upon in a clinical context.
- Individual research results will not be disclosed to the participant or their family members.
- The research result will be validated in a clinical environment – Familial Cancer Service or a local similar service according to where the patient was consented or where appropriate. TR-ANZGOG investigators will help facilitate patient contact and re-testing as deemed appropriate by the EDP Panel.
- TR-ANZGOG will be responsible for providing identifying information to the treating clinicians to facilitate participant contact and re-testing in the clinical arena.
- Research results that do not have a health implication for the participant will not be disclosed to the participant or their family members.
- The participant will not need to give their explicit consent to be contacted if a research result has a health implication for them or their family. This is because it could be considered unethical, not to provide the opportunity of testing and possible treatment, based only on information relevant at that moment in time. Instead the patient will be approached and asked, in a clinical environment, if they consent to further investigation or testing.

The requirement from the National Statement and the response from TR-ANZGOG for each section are shown below.

Requirement

Section 3.2.15

Where proposed research involving the use of human biospecimens may reveal information that may be important for the health of the donor(s), their relatives or their community, whether anticipated or incidental to the scope of the research, researchers should prepare an ethically defensible plan to describe the management of any proposed disclosure or non-disclosure of that information. This plan must be approved by an HREC and, in reviewing this plan, the HREC should consider:

(a) The circumstances in which the biospecimens were obtained, including the type of consent provided and the manner in which the consent was obtained

Response:

Participants who give their consent will do so knowing that their biospecimens and data may be used in future unspecified research and that if clinically significant information is obtained, it may result in them being re-contacted to have test results confirmed. These tests will be performed in an accredited pathology laboratory, and that although unlikely, it is possible that research using their sample may identify genetic information that may have implications for them and their family. These points will be clearly stated in the PICF.

(b) The likelihood of the research generating information that may be important for the health of the donor(s), their relatives or their community

Response:

It will be clearly stated in the PICF that it is unlikely that a researcher will find a significant research finding that has a health implication for them, or a family member.

As the sample is collected for future unspecified research, it is unknown if and when the sample will be used in a research study, therefore the likelihood of research generating information that may be important to the health of the donor or their blood relative is small.

Also, genetic testing guidelines having been changed in Australia so most ovarian cancer patients (< 70 year old) are now eligible for referral to an FCC, so many of the women in TR-ANZGOG are likely to be referred to an FCC as part of usual care.

(c) Whether a recognised intervention exists that can benefit or reduce the risk of harm to the donor(s), their relatives or their community from any health impact revealed by this information

Response:

In the event that a research finding that has known health implications for the donor or their blood relative is returned to TR-ANZGOG it will be referred to a team of experts who will discuss a plan for the involved participant. This plan will involve confirming the research result using a clinically validated test in an accredited facility. If clinical testing confirms that an actionable mutation has been found, then an intervention will be planned. The participant or next of kin will be contacted by the treating specialist physician or by a centralised genetic counselling facility or the equivalent in their local setting, whichever is deemed more appropriate by the team of experts.

(d) The resource requirements and infrastructure in place to support the return of information of the kind referred to in (b) and (c) in an ethically appropriate manner

Response:

Please see 'Plan' above.

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(e) Whether participants will be given a choice to receive such information

Response:
The PICF states that participants will be alerted to the fact that a finding that may be of relevance to their health has been made, and they will be given the choice whether to discuss the situation with a relevant health professional. Participants will always be contacted if a medically significant finding has been discovered, however, they have the choice to decline any further intervention.

(f) Whether there is a pathway to identify and recontact the donor(s), their relatives or their community, taking into account the relationship between the researchers and the donor(s), if any

Response:
There is a pathway to identify and recontact the donor.
The identity of the participant is not disclosed to researchers as all TR-ANZGOG samples and data are coded. Only the relevant staff of TR-ANZGOG will be able to re-identify a study participant. As part of the EDP Panel TR-ANZGOG will communicate the participant's identity to the appropriate clinicians and genetic counselling service. The treating specialist physician or genetic counselling service will contact the donor or their nominated next of kin. TR-ANZGOG will facilitate the process, but researchers themselves will not contact the donor.

(g) The potential for sampling or coding errors that may compromise the certainty that the biospecimens came from a particular donor

Response:
To confirm the donor identity, a new sample will be taken from the participant and tested in an accredited clinical environment. If this is not possible, then other independent sources, such as the Pathology Department, may be used for tissue acquisition to confirm donor identity.
TR-ANZGOG may collect serial blood samples from our participants and a second stored blood sample may also be used to confirm donor identity if other options are not available.

(h) Whether the findings of specific tests being undertaken as part of the research have been produced or validated in an accredited laboratory

Response:
If a researcher reports a result which may have a potential health implication the EDP will be initiated. The panel of experts will decide if the research result warrants further investigation and if so, will further action the EDP and undertake independent validation in an accredited laboratory. Only findings that have been produced or validated in an accredited laboratory will be reported to the research participant by the clinician or genetic counselling service.

(i) Who will take responsibility for any subsequent care requirements?

Response:
The clinicians that are involved in the patient's cancer care and others that may be designated by the expert EDP Panel will be responsible for on-going care requirements.