**VERSION CONTROL COVERSHEET**

**TR-ANZGOG Recommended Optimal Biospecimen Collection**

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| **APPLIES TO SECTION:** | * All |
| **DOCUMENT NUMBER:** | * 6.1.1 |
| **PURPOSE:** | * To provide guidance on the minimal biospecimen requirements needed to facilitate translational research beyond the trial’s completion |
| **CREATED BY:** | * Claire Davies/ Anna De Fazio |
| **CREATION DATE:** | * 31 Jan 2019 |
| **ADVISORS CONSULTED:** | * Steering Committee, Consensus Workshop (dedicated specimen collection group – scientists, pathologists, biobankers, consumers, coordinator), Board. Compared with sector examples for alignment (INOVATe, AOCSII, Mater Research, WIMR Gynbank, Cancer2015, COB Lifehouse biobank) |
| **REVIEWED BY:** | * Steering Committee |
| **REVIEW DATE:** | * 4th Feb 2019 (S/C), Mar 2019 ASM (S/C working group), July 2019 (Board), 11 Nov 2019 (CW), 17 Sept 2020 (S/C) |
| **LEGAL REVIEW REQUIRED?** | * No |
| **IF SPECIALIST REVIEW STILL REQUIRED, WHOM?** | * Final approval by S/C required, including process of deciding where dedicated TR-ANZGOG specimens need to be collected as trial requirements do not meet recommended minimal collection |
| **VALID PERIOD:** | * Sept 2020-Sep 2022 |

**Version Control:**

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| **Version** | **Date** | **Reason for Change** | **Date Effective** |
| 1.0 | 31 Jan 2019 | New. Provided to S/C for review (including challenges and proposed solutions). F/U survey circulated as requested. Minimal response. S/C working group met at ASM 2019. | Draft |
| 1\_draft | 7 June 2019 | Format revised. Now includes summary of survey responses. | Draft |
| 1\_draft | 29 Oct 2019 | Clean version provided for Consensus Workshop, including background to recommendations and sector comparisons. | Draft |
| 1\_draft | 12 May 2020 | Inclusion of Biospecimen Acquisition wording for Protocol (based on OBER template), outlining collection methods.  Rationale for each sections’ recommendations removed | Draft |
| 1.2 | 24 May2020 | Combination of previous two versions ie. inclusion of rationale section after recommendations. Protocol wording (OBER template) at end of document.  Feedback from CW incorporated. | Draft |

**Approved by** *Pending by SC as at 25Aug2020*

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| **Name** | **Position** | **Signature** | **Date** |
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**Recommended TR-ANZGOG optimum biospecimen collection**

**(Clinical trial dependent):**

Representative *tumour* tissue sample/s (order of preference):

1. Archival FFPE block, primary and/or relapse
2. Temporary retention of FFPE block to create Tissue Microarray (up to 100 FFPE cores in duplicate per block) *eg* from each specific cohort of ANZGOG clinical trial participants
3. If FFPE block not provided: Unstained slides, Cores and/or Curls
   * Unstained slides: IHC – 10 x 4 um unstained slides; DNA – 6 x 10 um
   * Cores: 4 x 1 mm punches
   * Curls: 6 x 10 um scrolls
4. Where feasible, Ascites, for example:
   * Purified tumour cells for future DNA/RNA extraction
   * Cell block for future IHC/ DNA/RNA extraction
   * Cytospin for tumour cell assessment
   * Establishment of permanent tumour cell lines (TR-ANZGOG- designated laboratories may freeze aliquots of centrifuged ascites in suitable media to facilitate the generation of these cell lines by researchers).
   * Future establishment of permanent lymphoblastoid cell lines (LCL’s)

*Blood*

Examples:

* 1 x 9 mL ACD sample (whole blood, white blood cells)
* 1 x 5 mL EDTA sample (Guthrie cards, plasma, buffy coats)

**Rationale**

The above table outlines the recommended optimal samples to collect per patient to ensure an adequate resource to facilitate future research. However, each clinical trial will differ in objectives and therefore, the specimens to be collected. Flexible guidelines are required to reach a balance between what is practical, useful and warranted use of resources without interfering with trial processes nor increasing patient burden.

Resources will be prepared for clinician support including tables outlining sample collection requirements, processing standard operating procedures (SOPs) and budget considerations, based upon desired research activity. For example, a larger blood sample may be required for immunotherapy trials than for other trials to acquire adequate lymphocytes from buffy coat.

Guidelines on collection time points must remain flexible to accommodate trial objectives, eg. baseline may be pre or post treatment or end of treatment may be taken months later if waiting for WBCs to recover.

It is recommended that all new ANZGOG trials incorporating TR sub-studies liaise with TR-ANZGOG during the trial development stage and when submitting grant applications to assist with methods, protocols etc and to ensure that the translational aspects are adequately covered in the budget.

Table 2: TR-ANZGOG blood samples and derivatives

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| Parent sample (per donor) | Product | Number of Aliquots | Aliquot Size |
| 1 x 9 mL ACD | Whole blood | 4 | 1 mL |
|  | WBCs | 3 | 1 mL |
| 1 x 5 mL EDTA | Guthrie cards | 2 cards | 40 uL |
|  | Plasma | 4 | 500 uL |
|  | Buffy coats | 3 | 500 uL |

The above recommended minimum blood collection tube types and volumes will provide a range of end products sufficient to facilitate future research. Blood will be required for germline DNA. Note that genome-wide association studies currently performed are primarily for ovarian cancer risk and potentially for pharmacogenomics.

Guthrie cards provide a back-up and can be used for QC eg Short Tandem Repeat (STR) profiling.

The future establishment of permanent lymphoblastoid cell lines (LCLs) would be invaluable for future research. This could potentially be outsourced to another entity eg. kConFab or NSWSB. Propose that feasibility for this processing is considered at a future date.

**Access to FFPE blocks for TMA construction**

The construction of trial cohort TMAs will facilitate efficient IHC studies.

Retention of the FFPE block would be ideal for full face sectioning to allow for heterogeneity and/or DNA/RNA extraction.

Inability to acquire block should not exclude trial participation, provided adequate tissue exists to meet trial requirements (eg. 20x unstained slides provided instead of block).

*Not all pathology laboratories will be able to release the blocks.* The Canadian Cancer Trials Group (CCTG) Tissue Bank developed an SOP with pathologists to send to the pathology department when requesting FFPE block/s. This SOP is akin to an MTA but less legalistic and provides the pathology department reassurance that approved procedures will be undertaken. Stipulations are included such as the number of cases that are requested, when they are required, duration of block retention and minimum/maximal guidelines for cutting/ coring.

If the above-mentioned SOP was not sufficient for block provision, TMAs could potentially be made in-house by pathology department for a fee. However, not all pathology departments will have TMA construction capability. However, all Anatomical Pathology departments will have a punch (for IHC control tissue blocks) that could be used to provide cores to TR-ANZGOG for TMA construction, where adequate tumour tissue exists, at the pathologist’s discretion.

FFPE blocks will be provided to TR-ANZGOG in a potentially identifiable format. However, the sections will go to researchers in a coded format only. If blocks were to be de-identified by removing the patient surname, there is both a risk (and added workload to the pathology department) in reliably re-labelling with surname upon return. Site coordinators will be provided with an SOP instructing to affix a label of the trial number over the name printed on the FFPE block.

NOTE: Consent must include that TR-ANZGOG laboratory staff may see patient identifiable information but researchers will only receive coded information.

**BIOSPECIMEN ACQUISITION, PROCESSING AND STORAGE GUIDELINES**

All biospecimens will be collected and stored in accordance with the ISBER best practices and Good Clinical Practice/Good Clinical Laboratory Practice regulations and guidelines..

If the participant consents to providing blood biospecimen/s for the ANZGOG-supported clinical trial as outlined in the Participant Information Sheet and Consent Form, arrangements will be made for the collection through standard trial procedures. The collection of additional, dedicated TR-ANZGOG samples may only be required where samples that are collected as part of the TR-ANZGOG-supported clinical trial would not be available for researchers following completion of the trial and associated sub-studies. Case-specific assessment may be required.

It will be the Pathologist’s decision (or their designate) whether formalin-fixed paraffin-embedded (FFPE) tissue may be allocated to TR-ANZGOG for the creation of Tissue MicroArrays (TMAs).

Processing of biospecimens will be in accordance with the TR-ANZGOG Biospecimen Processing Manual unless otherwise agreed upon between the TR-ANZGOG Trial Support and Sample Access Committee and the trial principal investigator at the time of trial protocol development.

Specimens will be labelled in a re-identifiable manner which will include the unique trial study number and a unique TR-ANZGOG identification number. Specimens will be coded in a consistent manner to indicate the source biospecimen (eg.. EDTA, ACD) and product (eg. white blood cells, serum). Labelling guidelines are included in the Biospecimen Processing Manual.

Cryopreserved biospecimens will be stored in a secure freezer in TR-ANZGOG-designated laboratories within Australia and New Zealand with restricted access. The temperature of the freezers will be constantly monitored. Biospecimens stored at other temperatures (i.e. cool or ambient temperature) will be stored in appropriate storage containers in a secured room with appropriate temperature and humidity controls within in the TR-ANZGOG-designated laboratories.

The monitoring system will alert members of staff (over a 24 hour period, 7 days a week) if the temperature of the freezers deviate outside their operating limits. Back-up freezers will be available if there is a freezer failure. Independent electrical supplies will provide energy for the freezers and all will be secured by the Institution’s generator. A biobank software system will be in place to record the storage and withdrawal of biospecimens for research purposes. This will provide an audit trail for biospecimens.

TR-ANZGOG dedicated laboratories will be responsible for the maintenance of records, as outlined in agreements to demonstrate quality assurance adherence.