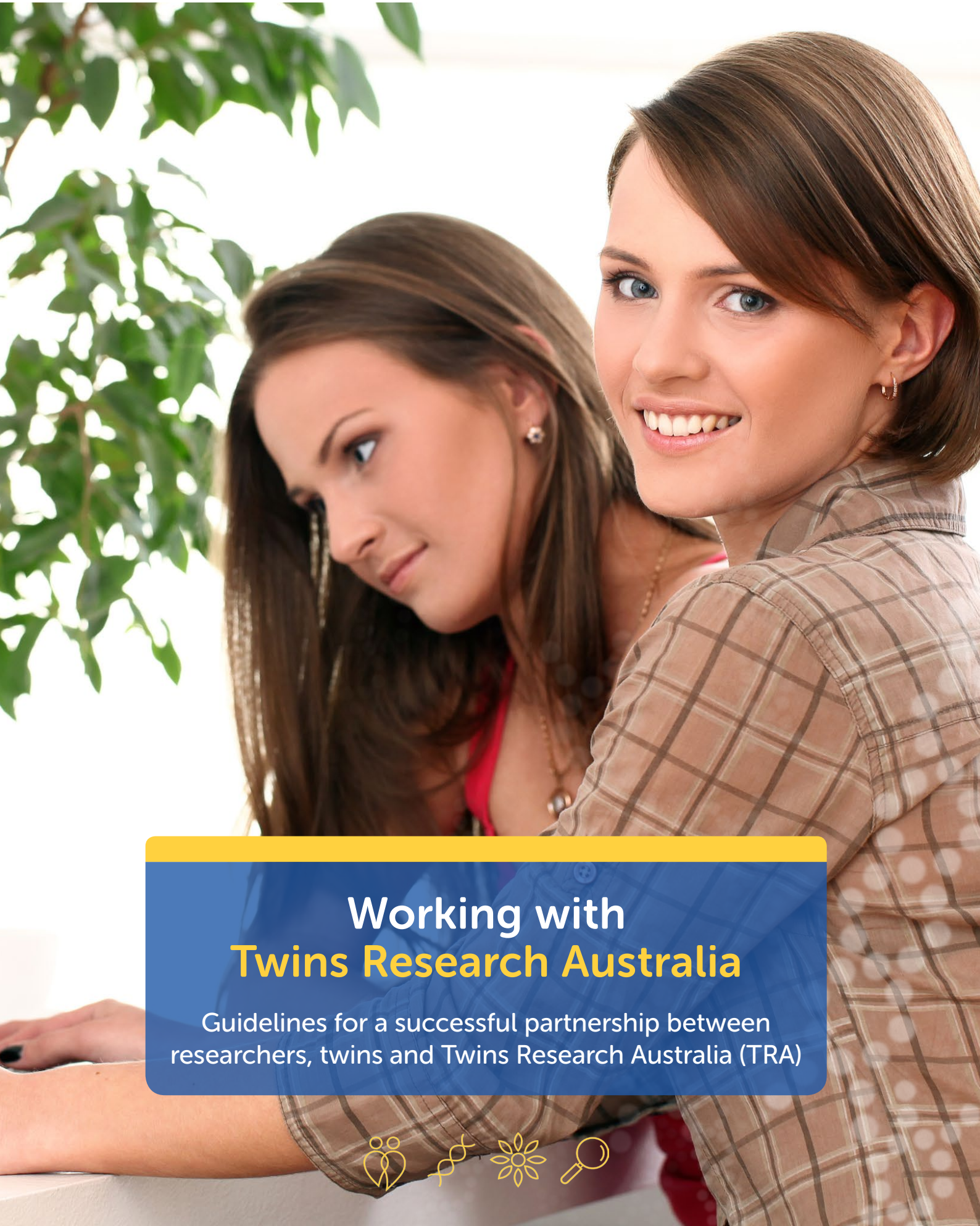
TWINS
RESEARCH AUSTRALIA



Working with Twins Research Australia

Guidelines for a successful partnership between researchers, twins and Twins Research Australia (TRA)

Table of Contents

B. Introduction

TRA's Vision:

Our vision is for a vibrant and unified global twin research community to improve health and medical knowledge for the benefit of all humankind.

We undertake research with twins to generate new knowledge to improve everyone's health and prevent disease.

TRA is committed to excellence in its interactions with researchers interested in accessing this resource. TRA enables and conducts research to achieve this vision.

Our core functions are:

1. We foster the **participation** of twins in research and support their wellbeing.
2. We undertake **twin research** and build research capacity and capability
3. We enable researchers to access the unique benefits that twins are able to offer to research
4. We maintain an up-to-date database containing contact details and baseline information for twin members willing to participate in research studies
5. We also seek to improve the lives of multiple-birth families by undertaking research of particular relevance to them, providing evidence-based resources, and advocating on their behalf.

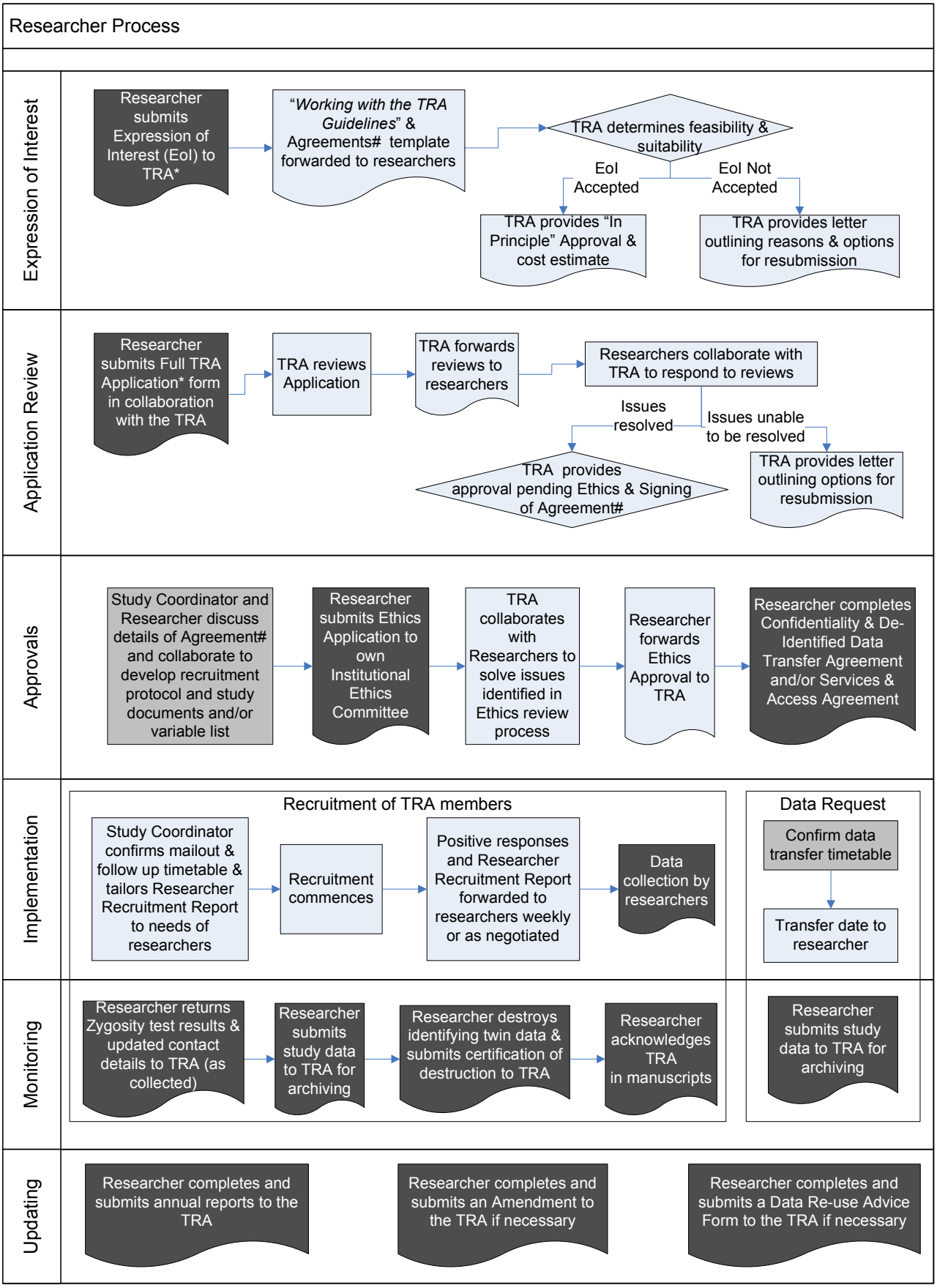
Aim of these Guidelines:

To help establish successful and productive research partnerships, using accurate communication of responsibilities and expectations for both TRA and the collaborating researchers.

This document is intended to facilitate clear and transparent discussions between TRA and researchers. It includes a flowchart outlining the steps undertaken in approving and rolling-out a study, a list of Researcher and TRA responsibilities, and detailed descriptions of important documents and processes in carrying out research with TRA.

If you have any questions, please call the Research Liaison and Study Coordinator on our free call number 1800-037-021 or from outside Australia on +613-9035-4412.

C. Application Approval Process



* Expression of Interest & Full TRA Application forms are available at www.twins.org.au or on request.
# The Services & Access Agreement and the Confidentiality & De-identified Data Transfer Agreement.

D. Summary of Researcher and TRA Responsibilities

Researcher Responsibilities	TRA Responsibilities
Application Review and Approval	
1. Submit **Expression of Interest (EoI)**. 2. Submit an **Application** for consideration using TRA **Application Form** (see Section E.1 for description and 3. Appendix 1 for form). All details must be provided in order to avoid delays in processing the **Application**. 4. 3. Understand future use of study data/samples in the development of long term data and sample management plans. 5. 4. Resolve any issues identified during the review process performed by TRA.	1. Provide the **Working with TRA Guidelines** and **Data Curation and Access Policy** to researcher. 2. Process **EoI** and **Applications** from researcher in a timely manner. 3. Provide letter stating "*In Principle*" Approval to all accepted EoI. 4. Review all **Applications** internally and externally (if appropriate), provide reviewers' comments to the researcher, and assist in solving all issues identified during the review process
Development of Approach Package / Study Documentation	
Projects involving recruitment or contact with Registry members	
1. Prior to submission to a relevant Human Research Ethics Committee (HREC), work with TRA to develop an **Approach Package**, the material used to invite potential participants to enrol in the study, including the **Information Sheet** (see Section E.2). 2. Prepare **Study Documentation** including the participant consent form (see Section E.2). TRA requires that the consent includes a clause requesting permission for potential future use of data/samples (see Section E.4). 3. Determine with TRA the timing of approach to eligible twins. 4. Determine with TRA the timing of the return of updated contact, participation and zygosity information.	1. Work collaboratively with researchers to develop an **Approach Package**. 2. Develop a study coordination plan detailing the timetable for approaching eligible twins, and **Study Flowchart** detailing the study recruitment steps. 3. Negotiate an agreed timetable for commencement of researcher / twin correspondence. 4. Negotiate an agreed timetable for completion of the **Participant Update spreadsheets**.

Researcher Responsibilities	TRA Responsibilities
Ethics Approval	
1. Submit application to HREC after the **Approach Package** and **Study Documentation** have been finalised and approval has been provided by TRA (see Section E.7). 2. Forward to TRA copies of all HREC correspondence including the application, amendments, approval letter(s) and approved study materials. 3. Inform TRA immediately in writing of any complaint and/or breach of ethics.	1. Maintain University of Melbourne HREC approval for TRA through the **Australian Centre of Excellence in Twin Research (ACETR) Program of Work**. 2. Maintain copies of all HREC correspondence 3. Forward any ethics complaint/ comment(s) received to the relevant researcher(s). 4. Collaborate with researchers in the development of project ethics submissions.
Access Agreements	
Projects involving recruitment or contact with Registry members	
1. Review the **Services and Access Agreement** (see Section E.6 and Appendix 2). 2. Ensure that parties named in the **Application** are familiar with and abide by the terms and conditions stated in the **Agreement**. 3. Return the signed **Services and Access Agreement** to TRA.	1. Forward amendments to the agreement, if requested by researcher, to the University of Melbourne Research, Innovation and Commercialisation Services. 2. Lodge the signed **Services and Access Agreement** with the University of Melbourne Research Office, which triggers transmission of data.
Projects involving access to existing de-identified data	
1. 1. Review the **Confidentiality & De-identified Data Transfer** Agreement (see Section E.6 and Appendix 3). 2. Ensure that parties named in the **Application** are familiar with and abide by the terms and conditions stated in the **Agreement**. 3. Return the signed **Confidentiality & De-identified Data Transfer Agreement** to TRA.	1. Forward amendments to the agreement, if requested by researcher, to the University of Melbourne Legal Services. 2. Lodge the signed **Confidentiality & De-identified Data Transfer Agreement** with the University of Melbourne Research Office, which triggers transmission of data.

Researcher Responsibilities	TRA Responsibilities
Study Rollout and Conduct	
1. Establish and maintain communication with twins according to agreed timetable. 2. Do not coerce/pressure twins to participate in a study. 3. Do not pressure subjects to keep going with a study on the basis that they have already started. 4. Do not approach twins independently for additional participation or for a new study without prior TRA approval. 5. Maintain Member ID as part of the study data set. 6. Inform twins if they are no longer required for participation or the study is delayed or cancelled. 7. Provide feedback to participating twins about study results via, e.g. direct correspondence, article in the *Twins* Newsletter, or a summary published on TRA website. 8. Provide TRA with a copy of all participant feedback and the date of distribution. 9. Complete the Participant Update spreadsheet with updated participant contact, participation and zygosity information according to agreed timetable. 10. Identify all non-TRA twins and approach them for recruitment with TRA within 30 days, using TRA brochures and registration forms.	1. Approach eligible twin members according to the agreed timetable. 2. Provide researchers with names and addresses (electronic format via a secure FTP server) of members who have provided permission. 3. Provide the researcher with a Recruitment Report on progress of recruitment. 4. Publish study feedback in the Twins Newsletter and a summary on the TRA website. 5. Provide researchers with a Participant Update spreadsheet to enable the researchers to provide updated contact and zygosity data, and incorporate into the **TRA Database**. 6. Provide copies of TRA brochures and registration forms to researchers on request for dissemination to non-TRA twins participating in the study. 7. Try to minimise the likelihood of participant burn-out (see Section E.8).
Fees	
1. Honour all invoices raised by TRA within 30 days of receipt.	1. Publish a detailed cost breakdown of all chargeable activities on TRA website. 2. Provide researchers with an estimate fee summarising the anticipated study costs. (continued on next page)

Researcher Responsibilities	TRA Responsibilities
	3. Inform researchers of cost alterations. 4. Recalculate cost estimates on request. 5. Maintain an accurate log of time and materials utilised. 6. Provide researchers with an invoice detailing all costs charged, i.e., final fee, within 30 days of the closest billing date of the TRA (30 June or 31 December).
Study Amendments	
1. Inform TRA of any planned changes to the study by submitting a Study Amendment form prior to commencement of any additional tests and/or procedures, any re-approach of twins, or any deviation from the original approved study. 2. Discuss with TRA further HREC approval and/or addition of information to the Approach Package provided to participants.	1. Review **Study Amendments** in a timely manner. 2. Reserve the right to solicit confidential advice or review of the **Study Amendment** (see Section I above).
Sub-studies and Secondary Analysis of Study Data / Samples	
1. Inform TRA of any sub-studies or secondary data analysis. 2. Ensure that any use of study data/ samples for potential sub-study or secondary analysis is under conditions consistent with the informed consent and HREC and TRA approvals. 3. Retain responsibility for negotiating any new collaborations or sub-studies arising from archived data/ samples. 4. Forward to TRA copies of correspondence/approval from the relevant HREC regarding the sub-study or secondary analysis of data/ samples along with the approved study documentation.	1. Encourage, and assist if possible, the use of data for sub-studies and secondary analyses. 2. Assist researchers in data and sample management. 3. Reserve the right to request an Application for any new research that might arise from a new collaboration or secondary analysis of data/samples.

Researcher Responsibilities	TRA Responsibilities
Data Storage and Security	
1. Maintain confidentiality of contact details and inform TRA immediately of any breach. 2. Do not transmit identifying data (see Section E.4) to any other party not named in the approved **Application** without TRA approval. 3. Do not utilise study data/samples (Section E.4) for market research or purposes other than those approved by TRA. 4. Destroy the contact information for participating members at the conclusion of data analysis. 5. Do not archive identifying data. 6. Forward all zygosity results and all updated contact details (within 30 days of the information becoming available) to TRA for inclusion on **TRA Database** in Microsoft Excel format (see Section E.3). 7. Forward data collected for the study to the TRA when it is cleaned for archiving (Section E.5)	1. Provide capacity for data management and archiving. 2. Provide information to relevant researchers about how to process and store study samples (i.e., biosamples). 3. Store cleaned study data sent by the researcher within the ACETR (see Section E.3).
Publications	
1. Acknowledge TRA in all publications arising from the study by including: This research was facilitated through Twins Research Australia, a national resource in part supported by a Centre for Research Excellence from the National Health & Medical Research Council. 2. Advise TRA of all publications preferably prior to publication. 3. Provide TRA with an electronic copy of each publication; e.g. by e-mailing a PDF to info@twins.org.au, within 30 days of publication.	1. Record all publications. 2. Report all publications in annual reports to the NHMRC and on website.

Reporting Responsibilities

4. Submit an **Annual Project Status Report** to TRA (usually by mid-November; date to be confirmed by TRA each year).
5. Provide participants with study feedback, such as brief summary of study findings or personalised results of tests and measures.
6. Provide TRA with a copy of generic feedback and/or a summary of the nature of personalised results and the date posted.
7. Provide a summary of study progress and results in the **Annual Project Status Report**.

1. Request an **Annual Project Status Report** to TRA by mid-November (specific date to be confirmed by TRA).
2. Publish an **Annual Report** (date to be confirmed by TRA)
3. Prompt researchers via the **Annual Project Status Report** to provide feedback to members and TRA.
4. Facilitate feedback through publication of a *Twins* Newsletter and maintain an active TRA website. The publication timetable for the Newsletter is variable and researchers will be informed by email when the call for articles has commenced.

Quality Assurance

1. Participate in Quality Assurance (QA) surveying activities conducted by TRA in relation to the study.

1. Undertake QA surveying of researchers to measure expectations and satisfaction, and to identify and rectify any problems.
2. During study rollout, undertake QA surveying of twins to improve satisfaction and positive response rates, and to ensure that the **Approach Package** has adequately informed the twins.

Dispute Resolution

2. If instigated, follow the Dispute Resolution process as outlined in the Governance section on the website www.twins.org.au
3. Seek advice on disputes from TRA Director, Coordinator or Advisory Board Chairperson (contact details on the website www.twins.org.au).

1. If instigated, follow the Dispute Resolution process.
2. Provide advice on dispute and try to resolve

E. Detailed Descriptions

1. Content of application

The **TRA Full Application Form** (see Appendix 1) requests the following:

1. Detailed plan of the intended study
2. Description of all tests and measures anticipated for the life of the study
3. Drafts of all survey/measurement tools
4. Draft **Approach Package** if project involves recruitment of twins (see Section E.2 for details)
5. Draft **Study Documentation**, including consent forms if project involves recruitment of twins (see Section E.2 for details)
6. Completed **Data Request Form** if project involves access to existing data (see Section E.4 for details)
7. All optional or planned additional phases and any plans for extending the study

The purpose of the TRA application process is to review the proposed project to ensure it is:

a) of scientific merit,
b) of significant value to the proposed area of research,
c) able to comply with the appropriate ethical guidelines,
d) able to be suitably answered utilising a twin model, and
e) an appropriate use of TRA facilities

TRA Management approves or rejects **Applications** at their discretion; prior award of funding does not obligate TRA to approve studies.

2. Content of approach package / study documentation

The **Approach Package** usually contains:

1. A signed letter or an email from TRA introducing the researcher and research topic (provided by TRA)
2. A detailed **Information Sheet** outlining the study and the steps involved in participation, written by the researcher in collaboration with TRA
3. A TRA Consent Form to record the Registry member's interest in participating and consent for contact details to be forwarded to the researcher (provided by TRA).

The **Information Sheet** must:

1. Clearly state the study burden on the participant including: number, anticipated length and location of all tasks, questionnaires, interviews, clinical testing sessions, further follow-up and other anticipated study protocols for the life of the study
2. Include an explanation of optional or planned additional phases or extensions of the study
3. Outline any benefits and/or risks associated with participation
4. Provide a timetable for and an explanation of the type of feedback participants should expect
5. Provide details of the approving HREC and a contact person for complaints
6. State that members are free to withdraw from the study at any time and to decline to answer any question or to undertake any test.
7. For studies in which twins are initially screened for eligibility for a further study, this information must be included so that an informed choice regarding potential involvement can be made
8. Describe the storage and transmission of data/samples generated by the study in the short and long term, and any potential extended use of the data/ samples by other researchers
9. Inform the twins that the data will be stored with TRA for potential extended use by other researchers.

Upon enrolment into the study, the researcher sends participants further information, the Study Documentation, which includes:

1. Consent forms
2. Additional explanatory material
3. Participant Information Statements as required by the local HREC
4. Survey tools, etc.

Example documents are available on the website at www.twins.org.au and directly from the Research Liaison and Study Coordinator.

3. TRA database

TRA maintains information regarding twin members' contact details, date of birth, medical conditions of interest and zygosity on a network-protected relational database, the Database, which is held on a secure server at the University of Melbourne. The process of maintaining up to date information is on-going, and the database is improved for all researchers when TRA is notified of any changes to twin member details established by researchers during the course of their study.

If mail sent to a member is "*Returned to Sender*", or if a telephone call has indicated that the member is no longer at the registered address, the member is marked

"Pending" and is removed from study invitations until located. TRA conducts regular tracing of all Pending members, which currently runs at 5% or less. TRA bears all costs for tracing Pending members.

TRA records any volunteered information regarding health status of twin members. TRA makes no assurances that this information is accurate or exhaustive. It is the researcher's responsibility to confirm such information if required for their study.

TRA collects information on each twin pair's self-reported zygosity at the time of their registration. As this data are usually based on either a parent's report or the twins' self-assessment, it cannot be assumed to be accurate. If accurate zygosity determination is critical for a study, researchers will need to undertake this determination. Assessment of zygosity by questionnaire is known to be accurate for about 95% of pairs.

Researchers are required to submit to the **TRA Database** any updates to contact details of twins gathered during the time that twin members are involved in a study, which help in the tracing and tracking service it provides to all researchers who utilise the resource. TRA also requests from researchers the results from DNA-based zygosity testing using biospecimen samples collected for a study, or if zygosity information is a by-product of genotyping performed on DNA from collected samples, so this data can be added to the **TRA Database**. Researchers are required to submit this information in the **Participant Update Spreadsheets** supplied by TRA according to the agreed timetable.

4. Data/samples management

Definition of Identifying Data and Study Data/Samples

A definite distinction is made between identifying data (names, addresses and telephone numbers) supplied to the researcher by TRA for the purposes of contacting eligible, willing twin members, and study data/samples generated from measures and tests conducted with participating twins.

Consent for Extended Use of Study Data/Samples

As a minimum, TRA requires researchers to include provision for the potential extended use of study data/samples when constructing consent forms and study documentation, and explain clearly to participants that their study data/samples may be used for other health related studies. This requires the inclusion of appropriate clauses in the informed consent documentation signed by the participant to provide permission for study data/samples to be utilised by other studies. For example:

Information Sheet:

> *The information you provide for this project will be a valuable resource for both current and future research. We would like to provide a copy of this information to Twins*

Research Australia (TRA) for use in future research. Your data will only be used in the future for research approved ethically and by TRA.

Your data will be stored securely and separately from any personal information that may identify you. TRA will store this data indefinitely in a coded form within the Australian Centre of Excellence in Twin Research at The University of Melbourne. The data you provide for this project may be linked with other data you have provided or may provide in the future. Your data will not be provided to researchers with personal information that may identify you without additional consent from you. We will undertake to protect your privacy within the limits of the law and follow State and Federal Government guidelines.

We would also like to inform Twins Research Australia of updates you provide to us about your contacts details and zygosity for the purpose of keeping their records up to date and maintaining contact with you.

Consent Form:

I consent to the researchers providing updated contact details to Twins Research Australia for the purposes of updating my record and maintaining contact.

I consent to the researchers providing study data to Twins Research Australia for possible reuse in future approved research, as outlined in the Information Sheet.

Alternatively, where it is not appropriate to include these items on the Project forms, TRA may arrange for a separate TRA Data Curation and Harmonisation Information Sheet and Consent Form to be sent to each participant. These projects will be required to explain on their Information Sheet that the separate Information and Consent Form will be sent to all participants.

Re-use of study data/samples

Re-use of study data/samples for subsequent studies is considered by TRA in two ways:

1. As a **SUB-STUDY**:

   This covers analysis of the study data/samples by the same research group, under the same Principal Investigator, within the scope of the original research application and protocol, e.g. further analysis of study data/samples by PhD and Honours students in the same research group.

2. As **SECONDARY ANALYSIS OF STUDY DATA / SAMPLES**:

   This covers any use of the study data/samples that departs from the purpose/s other than those stated in the original Application and Protocol, e.g. use of study data/samples by another research group, or use of study data/samples to investigate a different area of research.

5. Data storage and archiving to facilitate further research

Long Term Storage of Study Data/Samples

In the interests of realising the full potential of research involving twins and minimising the burden to participants, TRA requires researchers to archive study data and consider long term storage of samples.

Lodgement of study data with TRA aims to encourage the building of new research and extension of existing research. It is also, in accordance with TRA's commitment to minimise the risk of Registry member burn-out (see Section E.8). Making study data available for future researchers reduces the need for fresh contact with members, and minimises costs associated with recruitment of participants. The conditions of use of the archived study data are as stated in the **TRA Curation and Data Access Policy**.

Researchers must provide a copy of the study data to TRA for archiving, under the conditions stated in the **TRA Services and Access Agreement**, and the **TRA Curation and Data Access Policy** (see Appendix 4). The timing of this archiving should coincide with the completion of the cleaning of study data by the researcher.

If researchers do not have access to an in-house facility to process and store biosamples, TRA can work with the researchers to find appropriate services. For details please contact the Research Liaison and Study Coordinator.

6. Access Agreements

TRA has two standard agreements covering the TRA/Researcher relationship. These are the **TRA Services and Access Agreement** and the **TRA Confidentiality and De-identified Data Transfer Agreement**.

The **TRA Services and Access Agreement** is a legal agreement to be entered into when researchers wish to recruit twins for a specific project from Registry membership. The **Agreement** outlines the parameters of the relationship between the research team and TRA (eg. Related fee conditions, responsibility of updating TRA on project progress, publications, updates to member details and contributing to the twin data and bio repositories), and the manner and terms in which identifying information of Registry members provided to the researchers is used by the research team. This Agreement is made between the University of Melbourne, as the administering body of TRA, and the Researcher's institution. It must be signed and lodged with the Melbourne Research Office (Legal Services)prior to the commencement of any recruitment or the transmission of data.

The **TRA Confidentiality and De-identified Data Transfer Agreement** is a legal agreement to be entered into when researchers request access to de-identified data stored in the TFCS data repository. It outlines the parameters within which the researchers can use the data and the obligations of the researchers to ensure TRA is updated on project progress, publications and study outputs and derived study outputs. This Agreement must be signed and lodged with the Melbourne Research Office (Legal Services) prior to a copy of the study data being provided.

Both standard Agreements are attached. Any amendment to the Agreements will necessitate the involvement of the University of Melbourne Legal Services group and could delay the transmission of data or commencement of recruitment.

It is the researcher's responsibility to become familiar with and abide by the terms and conditions stated in the Agreement. The signatory of the Agreement acknowledges responsibility for ensuring that all parties named in the application are familiar with and abide by the terms and conditions stated in the Agreement.

7. Ethics approval

The NHMRC National Statement on Ethical Conduct in Human Research emphasises each "institution's responsibilities for the quality, safety and ethical acceptability of research that they sponsor or permit to be carried out under their auspices". This statement includes those institutions whose "employees, resources and facilities are involved in research" pp4. TRA is therefore required under these guidelines to ensure the ethical conduct of its own activities and the associated activities of research studies for which it recruits.

The Human Research and Ethics Committee (HREC) of the University of Melbourne has approved the overall operations of TRA through the ACETR Program of Work, including all processes and policies. These processes and policies are outlined in the ACETR Operations Guide, available from the TRA website.

All research studies auspiced by TRA must obtain local HREC approval and include the HREC contact details in participant information documentation. This submission must be made after TRA has provided approval for the study, and all Approach Package and Study Documentation is finalised. A copy of the ethics submission and of all correspondence regarding the submission including any subsequent amendments must be forwarded to TRA.

8. Minimising the likelihood of Registry member "burn-out"

The core function of TRA is to realise the full potential of research involving twins. To achieve this, TRA must ensure that twin members are approached in a manner that does not jeopardise their involvement in future studies. Serious consideration is given during the review process regarding the potential participation of twins who have been in recent studies. TRA takes into account the level of burden of the study and

tries to prevent excessive approaches to twins for involvement in research studies.

To reduce participant "burn-out", TRA usually allows a 6 month gap between invitations to members to participate in research studies. When concurrent studies with overlapping criteria seek to approach twins, TRA negotiates plans delineating separate pools of eligible twins.

When appropriate, researchers are encouraged to share information or collaborate with one another on certain aspects of their respective ventures. This balancing of the needs of twins and researchers might mean that some researchers are delayed in accessing certain groups of twins.

D. Appendices

Appendix 1: TRA Full Application Form

Appendix 2: TRA Services and Access Agreement

Appendix 3: TRA Confidentiality & De-identified Data Transfer Agreement

Appendix 4: TRA Curation and Data Access policy