Title: GUIDANCE Recruitment, screening and enrolment of research participants

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Institution name: Melbourne Children's

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These signatures confirm the reviewers agree with the technical content of the document and that this document is approved for implementation at the Melbourne Children's Campus.

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This document is effective from the date of the last approval signature and will be reviewed in two years.

Document History

Revision	Modified by	Change No.	Description of Change
1.0	CRDO – Fiona Williams	N/A	New Issue

Contents

1. PURPOSE

Recruitment of participants for a research project (known as a study) is the process where people are identified and contacted for further discussion, provide informed consent, are screened and (where eligible) enrolled in a study. Recruitment is crucial to the success of any study - planning for recruitment and developing strategies to maximise recruitment should take place prior to study commencement. A poor or non-existent recruitment strategy increases the likelihood of:

- poor levels of referrals to the study
- referral of people who do not meet the entry criteria
- participants not completing the study (due to withdrawal or loss to follow-up).

This guidance document describes the necessary steps for fulfilling the regulatory and clinical requirements involved in participant recruitment, enrolment (obtaining consent) and screening (confirmation of eligibility against inclusion and exclusion criteria).

2. SCOPE AND RESPONSIBILITY

This guidance applies to the activities involved in recruiting, enrolling and screening potential participants for inclusion in studies at the Melbourne Children's campus. This guidance does not detail the activities involved in obtaining informed consent – refer to the Royal Children's Hospital (RCH) procedure "Informed Consent in Research" (RCH 0499), available on the RCH intranet

3. APPLICABILITY

This guidance applies to research personnel involved in conducting human research at the Melbourne Children's campus.

4. PROCEDURE

4.1. DEVELOP AN OVERALL RECRUITMENT PLAN

The study protocol should provide an outline of the proposed recruitment plan and should identify:

- The target population for potential study participants based on the specific inclusion/exclusion criteria listed in the study protocol
- The recruitment timeline for the study (i.e. the time period available for recruitment). As part of finalising the study protocol, a realistic time frame for recruitment should have been determined - this is often based on historical or current data about the target population. For example, to determine the number of RCH patients with a current or previous clinical condition, non-identifiable information can be extracted from the RCH electronic medical record (Epic)* using the "Slicer Dicer" function.
- Appropriate recruitment strategies for the study (i.e. where the target population can be found along with appropriate methods for reaching this population). For example, for clinical research, this could include Epic*, clinic lists, clinical referrals or social media. For public health research, it could include school-based recruitment, random digit dialling, advertising or social media. If the protocol provides only high-level (broad) information on recruitment strategies, more detail should be provided in a separate document (i.e. which strategy will be undertaken when, how and by whom).

  * Prior to HREC approval, patient data in Epic can only be accessed in non-identified form. Following HREC approval, and once the study has been added to Epic and the patient attached to the study, identified data can be accessed.

Recruitment is often seen as the first step in the informed consent process. Potential participants may first learn of the study through recruitment materials (e.g. invitation email/letter, flyers/brochures/posters, website or social media site). Therefore, any recruitment materials to be viewed by potential participants and the general public must be submitted for review by the Human Research Ethics Committee (HREC) along with the study protocol, the participant information and consent documents and details of the recruitment methods. All documents must receive ethical approval and institutional (governance) authorisation prior to recruitment commencing.

There will be other requirements to be met before recruitment of potential participants can commence and a non-exhaustive list is provided below. See also the RCH "Investigators Responsibilities in Research" (RCH0498), available on the RCH intranet.

- Studies that are commercially sponsored or multi-site studies led by a coordinating centre may require sponsor or coordinating centre approval before commencing.
- The principal investigator should document their approval for the commencement of recruitment for the study. To ensure all is in place, go to the CRDO website to review the CRDO SOP "Study Start up" (as of JAN 2019 this is in progress) and to locate and complete the "Checklist for Study Start".
- The study must be added to Epic if it (i) involves RCH patients*who will be actively involved in the study (i.e. excludes research which is observational or just medical record review) and who will have procedures or services conducted at RCH or (ii) is a clinical trial of an investigational drug or device which will be given at the RCH (see RCH procedure "Epic: Appropriate Use for Research"). A patient of RCH is defined in the procedure as "Any child/young person admitted to RCH, attending RCH clinics or the emergency department.

Note that children/young people attending RCH for a Research 3T MRI or those attending 4 West (MCRI space) are not automatically considered RCH patients. At the Principal Investigator's discretion these participants can still be entered into Epic and associated with the study).

- In addition for clinical trials (i.e. a study that prospectively assigns participants to an intervention):
    - Ensure that the clinical trial has been registered on a publicly accessible clinical trial registry before the first participant is recruited (refer to the CRDO SOP "Clinical Trial Registration of Investigator-Initiated Trials (IITs)".
    - For drug/device trials, ensure that the TGA has been notified of the clinical trial and participating sites under the Clinical Trial Notification (CTN) scheme (where applicable) and that the trial has been added to Epic (as detailed previously).

4.2. IMPLEMENT THE RECRUITMENT PLAN

4.2.1. Pre-screen

Following ethical approval and governance authorisation of the study, the study team may start to identify potential participants.

Studies vary in the complexity of how eligibility is assessed. While for some studies, it is possible to determine full eligibility prior to informed consent, other studies will require a multi-step assessment process (i.e., the person meets initial criteria but additional procedures or study specific testing are required to finalise eligibility - this cannot be undertaken until informed consent has been provided). Additional testing after consenting is sometimes required for clinical trials.

For the purposes of this guidance document:

- **Pre-screening** refers to the evaluation of generalised characteristics prior to consent and screening to initially determine eligibility (prior to HREC and governance approval only de-identified data should be accessed). The characteristics may be determined from the medical record, a referring clinician or other sources as appropriate to the study (including self-referrals by potential participants), but not via any procedures undertaken specifically for the study. Identifiable data may be accessed if the researcher is part of the clinical team caring for the potential participant.
- **Screening** refers to information collected specifically to assess eligibility for the study (i.e. that is in addition to clinical care). Some examples of this are: testing cognition, assessing level of physical function, taking blood samples, and requesting medication history. As such this information is always collected after consent has been obtained.
- **Enrolment** refers to participants who have provided informed consent, have been screened for study eligibility and have been deemed eligible. **Note that for clinical trials, enrolled refers to participants who have been assigned to the trial intervention.**

Initial eligibility can be determined from the medical record (e.g. Epic), a clinician's referral to the study**, telephone contact**, website registration or other sources as appropriate to the study. During pre-screening, the person may be excluded due to one or more of a range of factors such as demographic information (e.g. age, sex), medical history, current or previous treatments.

** Note that the study should be introduced to the potential participant by an individual who, by virtue of his/her position, would normally have access to the potential participant's confidential information; this may be the researcher.

A **Pre-screening Log** (template available on the CRDO website) should be maintained in the Investigator Site File to record limited details of those who were pre-screened but not enrolled in the study, along with the reason for exclusion. This allows study personnel to track reasons and trends for non-inclusion in a study and check whether potentially eligible participants are being missed. Completion of a pre-screening log is also useful to ensure that those already excluded or who declined participation are not re-contacted. As the information is collected without consent being sought or granted, the information recorded on a Pre-Screening Log should:

- Involve limited collection of data particular with regards to personal and health information – only that data that is truly necessary for the study should be collected.
- Not be stored in identifiable format, particularly where health information is recorded (it may be stored in re-identifiable format e.g. initials and date of birth).

4.2.2. Consent, Screen and Enrol

For those not excluded during the initial stage (Pre-screening), the next step is to attend a Screening Visit (also known as a Baseline Visit) at which consent is obtained (refer to the RCH procedure "Informed Consent in Research" [RCH 0499]). A **Consent, Screening and Enrolment Log** (template available on the CRDO website) should be maintained to record identifying details of all participants who have consented. The consent date should be recorded along with the enrolment date (if enrolled) - if not enrolled, the date and reason for screen failure should be detailed, in accordance with ICH 4.1.1.29. This log demonstrates the lack of bias in the selection of participants and the investigators attempt to enrol a representative sample of participants.

At the Screening Visit, final checks against the inclusion and exclusion criteria will be undertaken to finalise the decision on the participant's eligibility for the study:

- Those deemed to be ineligible should be classed as a Screen Failure and will not continue in the study.
- Those deemed eligible are considered enrolled (*except in clinical trials where participants are considered enrolled only after they have been assigned to the intervention).*
    - Participant inclusion in the study should be documented in the participant's source document (which may be the RCH Epic record or participant's study [shadow] file).
    - Where clinically relevant, patients of RCH must be associated to the study in Epic – this is mandatory for participants in clinical trials involving an investigational drug or device.

4.2.3. Monitor the effectiveness of the recruitment plan

It is important to regularly track (monitor) actual enrolment into the study against the target enrolment. The principal investigator and sponsor or coordinating centre (where applicable) should be kept apprised of actual versus target enrolment.

If actual enrolment falls behind target, alternative recruitment strategies should be identified. Alternative strategies and any materials should be submitted for ethical and governance review.

Where recruitment may exceed the target listed in the protocol submitted for ethical approval, HREC and RGO must be notified. Where recruitment may exceed that specified in the approved protocol, a protocol amendment should be submitted for review and approval.

Recruitment information provided in clinical trials registries should also be updated as needed:

- For ClinicalTrials.gov, notice of changes in recruitment status must be provided as soon as possible, but no later than 30 days after such changes. This includes changes to individual site status, overall recruitment status and completion date.
- For ANZCTR, the entire record should be updated at least every 12 months.

5. GLOSSARY

Clinical trial
The World Health Organization (WHO) definition of a clinical trial is "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes".

Governance Office
The Office or coordinated function within an Institution which is responsible for assessing the site-specific (institutional) aspects of research applications, making a recommendation to the District CEO / delegate as to whether a research project should be granted authorisation at that site, and overseeing that authorised research at the site meets appropriate standards (research governance).

Inclusion and Exclusion criteria

- Inclusion criteria - A list of requirements, that individuals must meet, in order to be eligible to participate in the study.
- Exclusion criteria - A list of requirements, any of which will exclude the person from participating in the study.

International Conference on Harmonisation (ICH)
International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator
An individual responsible for the conduct of a study, ensuring that the study complies with GCP guidelines.

- If a study is conducted by a team of individuals at a study site, the investigator is the responsible leader of the team and may be called the Principal Investigator (PI). In this instance they may delegate tasks to other team members.
- If a study is conducted at more than one study site, the Principal Investigator taking overall responsibility for the study and for the coordination across all sites is known as the Coordinating Principal Investigator (CPI); the Principal Investigator at each site will retain responsibility for the conduct of the study at their site.

Note that for investigator-initiated research, the PI or CPI leading the research takes on responsibilities of the Sponsor and the term "Sponsor-Investigator" should be adopted to highlight the combined sponsor and investigator role.

Melbourne Children's
This term is used to encompass all staff from The Royal Children's Hospital, Murdoch Children's Research Institute and Department of Paediatrics University of Melbourne.

Participant Shadow File
Individual participant folder labelled with the name of the study in a consistent format with the main site file, and should contain:

- Signed Informed Consent Form (photocopy or original)
- Test results to confirm eligibility, if applicable.
- Documentation from study centre showing patient has been randomised (if applicable)
- File Notes related to the participant, e.g. protocol deviations
- Photocopy of letter to GP (if applicable)

Pre-screening, Screening and Enrolment

- **Pre-screening** The evaluation of generalised characteristics prior to consent and screening to initially determine eligibility (following ethical and governance approval of the study). The characteristics may be determined from the medical record or other sources as appropriate to the study (including self-referrals by potential participants), but not via any procedures undertaken specifically for the study.
- **Screening** This involves collection of information that is in addition to clinical care, it is collected for the reason of assessing eligibility for the study. Some examples of this are: testing cognition, assessing level of physical function, taking blood samples, and requesting medication history. As such this information is always collected after consent has been obtained.
- **Enrolment** – Participants who have provided informed consent, have been screened for study eligibility and have been deemed eligible are considered enrolled in the study, *except in clinical trials where participants are considered enrolled only after they have been assigned to the intervention.*

Recruitment
The process where people are identified and contacted for further discussion (where potentially eligible), provide informed consent and are screened and (where eligible) enrolled in a study.

Screen Failure
Where the person has provided consent after being fully informed of the study, and has been found to be ineligible, either because the inclusion criteria have not been met, or an exclusion criteria has been met.

6. REFERENCES

6.1. External

- Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2) annotated with TGA comments https://www.tga.gov.au/publication/note-guidance-good-clinical-practice

7. ASSOCIATED DOCUMENTS

7.1. Procedures

- Investigators Responsibilities in Research (RCH0498) - see RCH intranet
- Informed Consent in Research (RCH 0499) - see RCH intranet
- Epic: Appropriate Use for Research (RCH Procedure) – see RCH intranet
- SOP Study Start up (CRDO) (in progress) – see CRDO website
- SOP Clinical Trial Registration of Investigator-Initiated Trials (IITs) (CRDO) – see CRDO website

7.2. Documents and templates (available on the CRDO website)

- Checklist for Study Start (CRDO)
- Pre-screening Log template (CRDO)
- A Screening and Enrolment Log template (CRDO)

DOCUMENT END