PoCoG
Psycho-oncology Co-operative Research Group

Study Management

SOP ID: SOP_2.0.0-Study Management-130202

SOP development and approval

SOP developed by	Date	Associated document(s)
M Peate PoCoG Research Program Manager	28/09/11	**SOP_2.3.1-StudyMgt-120202-SWOT.docx**
M Peate PoCoG Research Program Manager	27/07/11	**SOP_2.3.2- StudyMgt-120104-SMC Roles Matrix Template**
M Peate PoCoG Research Program Manager	30/09/11	**SOP_2.3.3- StudyMgt-120831-Example budget**
M Peate PoCoG Research Program Manager	04/02/12	**SOP_2.3.4-StudyMgt-130222-Site_Startup_Checklist**
M Peate PoCoG Research Program Manager	04/02/12	**SOP_2.3.5-StudyMgt-130222-Study_Startup_Checklist**
M Peate PoCoG Research Program Manager	23/01/13	**SOP_2.3.6-StudyMgt-130123-Study_Audit**

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Supersedes documents: N/A

SOP Revisions

Approved by:	Date	Signature (only required for PoCoG hard copy)	Description of change(s)

Date Administered: 17/02/2012
Recommended date for review: 17/02/2014

Foreword

The Psycho-oncology Cooperative Group (PoGoG) has developed a program of quality assurance for psycho-oncology research. PoCoG's Quality System requires documentation of both management and procedural activities. This guidance document "Study Development" provides a standard working tool that can be used to develop a study from a concept.

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Table of Contents

Overview 4
Purpose 4
Scope 4
Guiding Principles 4
Definitions and Abbreviations 5
Qualifications and Responsibilities 6
1. Procedure 8
1.1. Concept development 9
1.2. Proposal development 9
1.3. Establishing a Study Management Committee (SMC) 9
1.4. Protocol development and approval 9
1.5. Applying for funding 10
1.6. Development of study manual and materials 10
1.7. Obtaining ethical approval 10
1.8. Study registration and other regulatory approvals 10
1.9. Site selection, enrolment and start-up 10
1.9.1. Site selection 10
1.9.2. Site preparation 11
1.10. Recruitment, management, and administration of the study 11
1.11. Data analyses and dissemination 11
1.12. Close-out 11
2. Records Management 11
2.1. Data Storage 11
2.1.1. The Master File and Master File Index 11
2.1.2. Archiving 12
2.2. PoCoG Records 12
3. Quality Assurance (QA) – templates, forms and checklists 12
3.1. Template: Strengths, Weaknesses, Opportunities and Threats (SWOT) Analysis 12
3.2. Template: Allocation of Roles Matrix 12
3.3. Template: Study Budget 12

Overview

This study management document is designed to guide the development of a research concept into a research protocol ready for implementation. It outlines the essential steps of the process for PoCoG endorsed trials, including the requirement for a study protocol, the establishment of a Study Management Committee, ethical and registration requirements, site agreements, and training of staff.

Purpose

This document provides a clearly defined pathway of research processes that meets scientific and ethical standards. The purpose is to guide researchers, who are at the concept stage of research development, through the processes required to conduct a research study and to provide tools to assist with the management of a research study.

Scope

This SOP is designed as a tool for setting up rigorous research studies and has been designed for Principal Investigators or a delegated authority (chief investigators, study managers or co-ordinators, support staff) developing a PoCoG study. It is intended and strongly recommended that PoCoG members also utilise this tool for other studies, however it is recognised that this may not be practical for all types of research.

Guiding Principles

Good clinical research practice

Good clinical research practice is conducted in accordance with applicable legislation and regulatory standards and this document has been guided by the following resources:

- International Conference on Harmonisation of Technical Requirements (ICH, http://www.ich.org/home.html),
- National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (henceforth referred to as the 'national statement', http://www.nhmrc.gov.au/publications/synopses/e35syn.htm),
- The Australian Code for the Responsible Conduct of Research (http://www.nhmrc.gov.au/publications/synopses/r39syn.htm),
- Note for Guidance on the Good Clinical Practice, Annotated with Therapeutic Goods and Administration's comments and the TGA's Australian Clinical Trial Handbook (http://www.tga.gov.au/industry/clinical-trials-handbook.htm),
- Declaration of Helsinki (http://www.wma.net/en/30publications/10policies/b3/index.html).
- Other guidelines as applicable (http://www.pocog.org.au/content.aspx?page=studyobligations)

Privacy and Confidentiality

The conduct of researchers and the manner research studies are undertaken must be in accordance with Australian federal and equivalent state privacy legislation. Participant confidentiality must be maintained at all times, except as required by law. Research protocols and study documents are often confidential and should not be provided to personnel not involved with a study.

Ethics

A research study must be designed to ensure the safety and health of research participants and to answer specific research questions, the details of which are outlined in the protocol. All PoCoG endorsed studies must have the relevant ethical, governance, and regulatory approvals prior to site activation/ participant recruitment.

Definitions and Abbreviations

Chief Investigator (CI)	A Chief Investigator has had a role in the development of the research proposal and protocol, is named as such on grant applications, and sits on the Study Management Committee.
Concept	A concept is the general idea or plan for a study and provides the fundamental idea behind the proposed research. A concept outline is a brief (one or two pages), clear summary that discusses, refines and supports a research question and an idea for a study. Typically it will include a statement of the importance of the problem, the potential impact of the intervention, scientific excellence and feasibility.
Coordinating centre	The primary site where the study will be coordinated or managed, typically where the Principal Investigator is based and/or where funding is administered.
Data Management Team	The data management team are designated members of the Study Management Team responsible for the quality of data collection, submission and processing.
Principal Investigator (PI)	The Principal Investigator is the investigator with primary responsibility for the research study and the leader of the Study Management Committee (see below). The PI is responsible for coordinating the CIs (and Site Investigators for a multicentre study). The PI is responsible for communicating with external bodies, including ethics committees, funding and regulatory bodies.
Proposal	A proposal is a plan or suggestion put forward for consideration or discussion. A research proposal is commonly written by one or more researchers and describes in some detail the program for investigation. This is more detailed than a concept, providing details of the question or problem being investigated, the limitations of existing research, rationale for the study, hypotheses, methodology and design, and timelines. The most common form of proposal is that which is submitted to funding bodies and is normally limited in the number of pages.
Protocol	A protocol describes the background, justification, objective(s), design, methodology, statistical considerations, organisation of the study, study duration, and a study plan on which the research is based. This includes specific details on eligibility and informed consent, schedule of procedures including adverse event reporting, the calculation of results and reporting standards (including a detailed statistical analysis plan). The study protocol enables the research to be undertaken at multiple locations using identical procedures, provides a common reference document all personnel involved in the conduct of the study, and identifies individual duties and responsibilities for the study. It is not restricted in length and should be as extensive as appropriate to detail all aspects of the study.
Quality Assurance (QA)	Assurance of quality is a set of preventive activities, which are focused on processes. In other words, all those planned and systematic actions that are established to ensure that the study is performed and the data are generated, documented (recorded), and reported in compliance with Good Clinical

	Practice (GCP) and the applicable regulatory requirement(s).
Quality Assurance Team	Quality assurance team are responsible for the quality assurance and control aspects of the study.
Quality Control (QC)	Quality control is a detection activity, which is focused on detecting problems. The operational techniques and activities undertaken within the quality assurance system are conducted to verify that the requirements for quality of the study-related activities have been fulfilled.
Statistical Team (ST)	The statistical team are responsible for the statistical aspects of the research, including devising a statistical plan as part of the protocol and analyses of study data.
Study Management Committee (SMC)	A committee composed of the PI and other CIs who will manage the study. The SMC are responsible for the general research issues, including safety reporting, ethical considerations, publication policy etc. The SMC will usually consist of a statistician, project manager/ study coordinator, representatives of the various disciplines involved in the study, and consumer representatives where appropriate. Also: Research Management Team (RMT)
Study Manual	The study manual outlines the step-by-step processes of the study. This may include example scripts for recruiting patients and the instructions for entering data into the database.

Qualifications and Responsibilities

A research study involves a number of stakeholders with distinct responsibilities outlined in Figure 1. This SOP focuses on the researcher's responsibilities in study development.

Principal investigator

The Principal investigator (PI) is responsible for the overall running of the study and is responsible for ensuring that the procedures outlined in this SOP are considered. The PI should be qualified by education, training and experience to assume responsibility for the proper conduct of the study and assembling a team with particular expertise to support the development and management of the study. PoCoG endorsed studies prefer PIs to be a member of PoCoG. Otherwise, at least one CI must be a PoCoG and assume PI responsibilities on behalf of the study team with respect to PoCoG endorsement requirements.

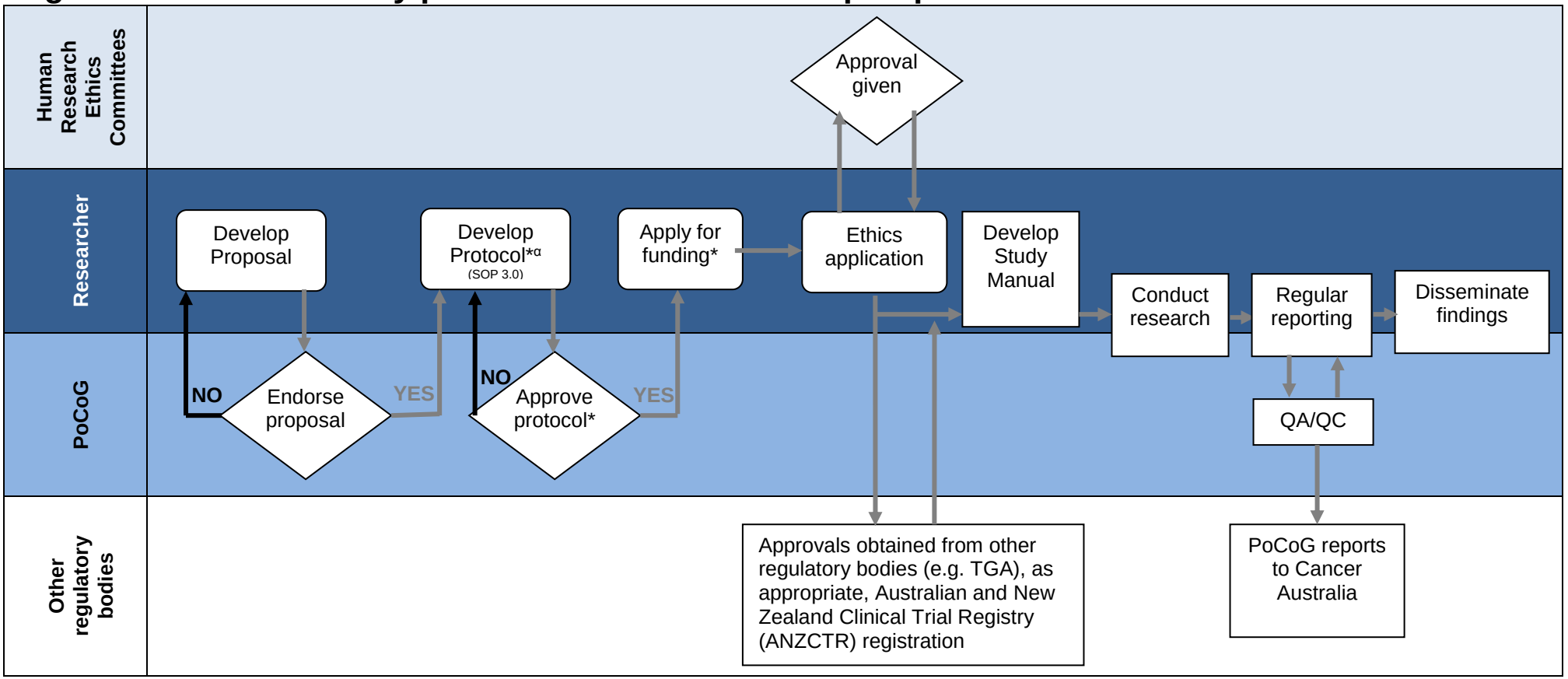
Chief Investigators

Chief Investigators (CI) are the team of co-investigators assembled by the PI to contribute to develop the research proposal, funding applications and become members of the Study Management Committee. CIs should also be qualified by education, training and experience to contribute valuably to the overall running of the study. CIs are responsible for contributing to the development the study protocol, conducting and managing the research study, complying with regulatory body requirements throughout the course of the study and dissemination of findings.

Site investigators

Multi-centre studies require designated Site Investigators (SI) for each of the recruitment sites involved in the study. These are often clinicians employed at the recruitment sites who agree to be responsible for all aspects of the study at their institution and ensure the study is conducted according to good clinical practice (GCP) guidelines. These responsibilities include ensuring adequate resources are available to conduct and complete the study according to the study protocol and ensuring the research personnel involved with the study at their site comply with local requirements, and applicable regulatory requirements.

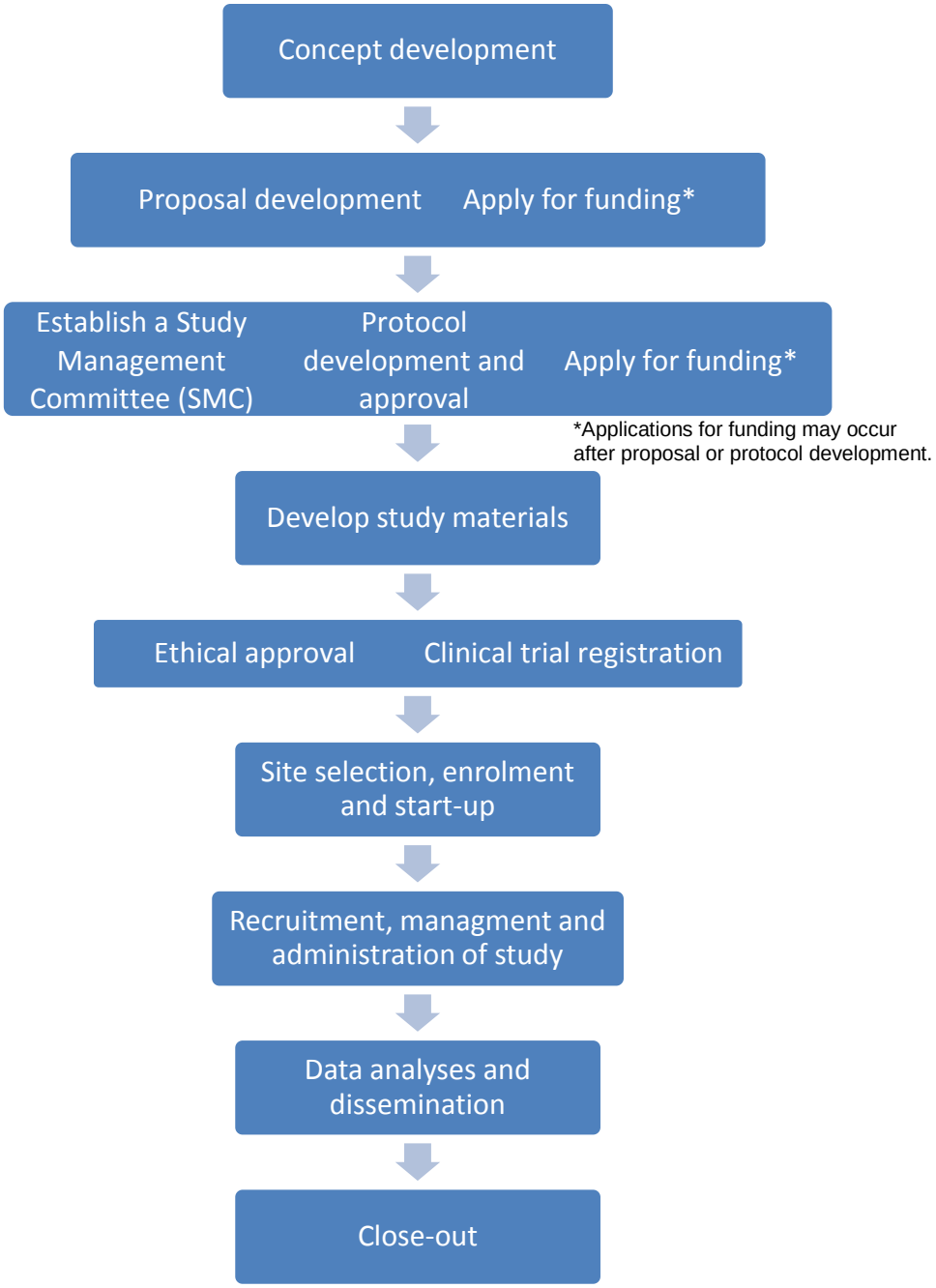
Figure 1: Research study processes: the researcher perspective



*Please note that the order of events may vary.
αPoCoG support is available for protocol development.

1. Procedure

The flowchart below provides a general order of events. The procedures below are ordered in the text to imitate the ideal scenario; however the practicalities of research may mean that order of the steps will be different.



1.1. Concept development

Concept development is the process of analysing and generating ideas around a project. The aim is to convert a research idea into a conceptual plan, considering the research question, relevance and meaningful outcomes, benefits and harms, feasibility, and the likelihood of obtaining funding. This process may be enhanced by using a Strengths and Weaknesses and external Opportunities and Threats (SWOT) analysis (SOP 2.3.1). This tool allows an examination of the internal and external factors that can support, inhibit, and progress the planned research. PoCoG offers regular concept development workshops (CDW) for members who would like support in developing an idea further (details are on the PoCoG website: www.pocog.org.au).

1.2. Proposal development

Proposal development is the next stage in the process and contains more detail than a concept. This is usually developed by the Principal Investigator (PI) and Chief Investigators (CIs), and provides the details of the question or problem, the limitations of existing research, defines the scope (or intellectual content), and rationale for the study. The proposal includes a description of the outcomes (objectives, study design, population, measures, feasibility and significance), study aims and hypotheses, methodology and design, and timelines. The level of detail included in a study proposal is necessary for the PoCoG Scientific Advisory Committee (SAC) to consider for endorsement. Further information of the endorsement process is available on the PoCoG website: www.pocog.org.au).

1.3. Establishing a Study Management Committee (SMC)

Following approval of the proposal by the SAC, the PI is responsible for assembling a Study Management Committee to oversee the conduct of the study. The SMC should include (where appropriate):

- The Principal Investigator and Chief Investigators (CI)
- Select Associate Investigators (AIs), or other specialists, to ensure a representation of each discipline involved in the study, if appropriate
- Statistician (PoCoG recommends that the statistician be a CI on the project or at minimum an AI or specialist consultant)
- Consumer representatives
- Site Investigators (or a representative)
- Project manager/ study coordinator

Members of the SMC should be allocated into teams with specific responsible for:

1. **Research management -** general research issues, safety reporting, ethical considerations, publication policy etc.
2. **Statistical management -** statistical aspects of the research, including the statistical plan (see SOP 4.0.0) and analyses of study data.
3. **Data management -** quality of data collection, submission and processing.
4. **Quality assurance -** quality assurance and control aspects of the study

Template 2.3.2 can be used to document the roles SMC members will play. The responsibilities of the members should also be clearly communicated, along with any commitments that may be expected (such as participation in regular meetings and teleconferences).

1.4. Protocol development and approval

The protocol describes the background, justification, objective(s), design, methodology, statistical considerations, organisation of the study, study duration, and a study plan on which the research is based. The protocol enables the research to be undertaken at multiple locations using identical procedures, provides a common reference document all personnel involved in the conduct of the study, and identifies individual duties and responsibilities for the study. The protocol also includes specific details on eligibility and informed consent, the schedule of procedures including adverse event reporting, the calculation of results and reporting standards (including a detailed statistical analysis plan). It is not restricted in length and should be as extensive as appropriate to detail all aspects of the study. The protocol needs to include a timeline estimate for each stage and activity. The activities

should be sequenced (and monitoring them should become part of the regular review process). Additional guidance on protocol development can be found in SOP 3.0.0.

1.5. Applying for funding

The next step is usually submitting an application for funding. The competitive nature of funding and the aims and priorities of funding bodies need to be kept in mind, and the SWOT analysis described in section 1.1 will be useful here. Specific application guidelines and your organisation's research office recommendations are also important to consider.

An important component of a funding application is the budget which estimated the costs of the research activities, including the costs of supplies and staffing. Each research study will require different resources, and once funded, the study will need to operate within these parameters. You will need to work through each stage of the planned study and think about what will have an expense attached and consider whether this is an appropriate item to request for funding. There is an example available to assist with developing a budget (SOP 2.3.3).

1.6. Development of study manual and materials

Study materials will need to be developed (e.g. investigator brochures describing the study, Patient Information Statement (PIS)/ Patient Consent Form (PCF), case report forms (CRFs), questionnaires, etc) prior to ethics submission. A study manual should also be developed which explicitly describes the procedural processes of the study. It is also pragmatic to develop a publication and public relations policy for the study which all investigators are aware of prior to commencement of data collection. At this point in time the study master file, where all study related documents are to be stored, should also be created (see below for more on the master file).

1.7. Obtaining ethical approval

It is crucial that research involving humans undergoes ethical review. Additionally, it is essential to have ethical approval so that results can be published in academic journals. PoCoG recommends contacting the local ethics committee for advice as each committee may have their own guidelines on use of the National Ethics Application Form (NEAF) and Site Specific Assessments. PoCoG administered studies should include the PoCoG Research Program Manager and Executive Director as sponsors on application, and any additional persons that will be provided access to the study files and data. Ongoing ethics approval is a requirement of PoCoG endorsement.

1.8. Study registration and other regulatory approvals

Study registration is becoming mandatory for clinical trials (including non-medical interventions) and is strongly recommended for all other studies. Please visit the Australia and New Zealand Clinical Trials Registry website (www.anzctr.org.au) for more information. Registration should occur prior to the recruitment of the first participant.

Regulatory approvals will not apply to most psycho-oncology studies, but in the event of the unregistered use of a treatment, investigators will need to obtain approval from the relevant authorities such as the Therapeutic Goods Administration (www.tga.gov.au). PoCoG requires evidence of approval from the relevant authorities as a condition of continued endorsement.

1.9. Site selection, enrolment and start-up

Site selection

As part of the selection of recruitment sites, you should only commence a study if there are:

- Adequate resources to complete the study – documented in resource declarations (this is often a requirement of ethics applications)
- Sufficient participants to meet the study objectives - documented with de-identified listings of subject recruitment and/or reports of estimated eligible participants
- Qualified and experienced study personnel - documented CVs

It may be worth having a short written summary explaining what your project is all about which you can send to the site investigators to elicit interest.

Site preparation

The process of site enrolment will involve training site investigators about study processes and establishing an understanding of roles and expectations. Generally this includes ensuring that:

- The budget, timelines, and processes have been negotiated – documented in clinical trial agreements or memorandums of understanding (MOUs) delineating roles and responsibilities
- Training processes have been set up – this should include a system for recording completion of training by site staff, including presence at the initiation meeting.
- Each site has the documents required to conduct the study. For intervention studies it is advised that a process to receipt the delivery of the intervention be applied.

1.10. Recruitment, management, and administration of the study

Once all the set-up is complete and all approvals have been obtained, the PI (or delegated authority) will need to notify the sites of the start date for recruitment, co-ordinate the study and associated administrative tasks. In many cases these responsibilities will fall on the study coordinator. Please refer to the specific SOPs that address the different elements of study administration.

1.11. Data analyses and dissemination

As part of this stage, investigators will begin data analyses and disseminate study results. Please refer to SOP 4.0.0.0 for advice on data management, SOP 8.0.0.0 for advice on developing a statistical analysis plan and PoCoG's policy and procedures manual for advice on presentation and publication of results (in addition to the study's own publication document).

1.12. Close-out

A study needs to be formally closed-out to ensure that all the study activities are completed. Once the final follow-up data has been collected the close-out process can begin. This includes notifying ethics committees that the study has closed, updating the clinical trials register and PoCoG. Please refer to SOP 10.0.0 for advice.

2. Records Management

PoCoG recommends that the study co-ordinating site keeps a study master file that is maintained by the study coordinator (or equivalent). It is the responsibility of the study coordinating centre to ensure that all required approvals and documentation is signed and completed prior to activation of the study at the site. The study coordinator will determine which documents in the master file list are required based on the scope or type of study and store the information in a study-specific master file index. For multi-centre studies, the study coordinator will be responsible for ensuring the sites have all the required documentation throughout the course of the study.

2.1. Data Storage

All study related data across all stages of project development should be stored in a secure manner (e.g. lockable filing cabinets and password protected computers).

2.1.1. The Master File and Master File Index

Each study should have a master file where the essential documents (as per section 8 of the ICH-GCP guidelines) are stored. This should include at least the following:

- Study protocol (including details of clinical trials registration) and amendments
- HREC approval documents
- Documentation of any other regulatory approvals
- Information brochures and patient information statement (PIS) documents
- Documents pertaining to financial arrangements (e.g. copy of grant application and associated letters)
- CVs of study personnel

- Study manuals and other documents relating to study procedures (e.g. Case Report Forms, questionnaires etc)
- Any documents relating to contractual or collaboration arrangements

A file tree that is currently used for PoCoG administered study documents is available from the Executive Office. All the data from the research project has a place in this system of storage – folders that are not relevant can either be ignored or deleted. It is important to maintain the numbering system allocated to folders to allow quick and easy access by different researchers to relevant documents as each has a particular place in which they are stored. The versioning of documents should also be very clear. This system is particularly useful when there are multiple researchers working on a project. Access to each of these folders should be considered.

The location of these documents and other data should be indicated in a secure master file index in a manner such that an auditor or inspector can access the information, as required by ICH-GCP. This file should also indicate whether different departments or unit hold specific sections of the master file.

The maintenance of the master file and index should be delegated to a member of the research team (often the study coordinator) and always be up to date. It is also recommended that the master file be checked annually for completeness. For more information refer to SOP 4.0.0 which addresses data management.

2.1.2. Archiving

According to NHMRC guidelines, study materials should be kept for at least seven years (for research data) or fifteen years (for clinical trial data) after completion of the study and then disposed of by secure destruction methods (which may include deletion of electronic data and shredding of information stored on paper). Archived information must be easily retrieved and available for review.

2.2. PoCoG Records

The study co-ordinator of a PoCoG endorsed study is also responsible for ensuring that, PoCoG's master file is current and contains the following:

- Study protocol (including details of clinical trials registration) and amendments
- HREC approval documentation
- Documentation of any other regulatory approvals
- Documents pertaining to financial arrangements, if relevant to PoCoG
- Any documents relating to contractual or collaboration arrangements, if relevant to PoCoG
- Regular reports on study progress

3. Quality Assurance (QA) – templates, forms and checklists

3.1. Template: Strengths, Weaknesses, Opportunities and Threats (SWOT) Analysis

This template (SOP_2.3.1) consists of a series of questions designed to assess the strengths, weaknesses, opportunities and threats in your study, which can be particularly useful to the Principal Investigator when designing the study.

3.2. Template: Allocation of Roles Matrix

Early in the study development process it is recommended that roles be allocated to investigators and research staff. This matrix (SOP_2.3.2) outlines the key roles and provides a mechanism by which they can be allocated.

3.3. Template: Study Budget

The study budget template (SOP_2.3.3) lists some of the common items that should be budgeted for in grant applications. Thought primarily designed for grants submitted to the National Health and Medical Research Council (NHMRC) it should be a useful tool for a range of projects and applications.

3.4. Checklist: Site Start-up

The site start-up checklist (SOP_2.3.4) lists some of the common steps involved in setting up a site for a study.

3.5. Checklist: Study Start-up

The study start-up checklist (SOP_2.3.5) lists some of the common steps involved in setting up a study.

3.6. Checklist: Study Audit

The study audit checklist (SOP_2.3.6) lists some of the important components of a study. It is designed to be used by management to audit a study that is in progress for compliance to the SOPs and in the broader sense, GCP.