PRIMARY CARE COLLABORATIVE
CANCER CLINICAL TRIALS GROUP

Protocol Checklist

Purpose

A protocol provides the background, rationale and objectives of a clinical trial or study and describes its design, methodology, organisation and the conditions under which it is to be performed and managed1.

This Checklist provides an overview of the details required in a protocol, and is designed to assist in the protocol development process, i.e. prior to submitting the protocol to a Human Research Ethics Committee (HREC).

Protocol Checklist

Cover Page

The study is clearly identified with:

- ☐ Title, Acronym, Grant ID number

Contact details (name, address, email and phone) of:

- ☐ Principal Investigator
- ☐ Administering institution

General information

The Study Management Team is easily identified:

- ☐ Use a table to list member names and role

Include a:

- ☐ Table of Contents
- ☐ List of abbreviations
- ☐ Glossary if required
- ☐ Footer on every page with:
  - i) Trial name and version
  - ii) Page number, and total number of pages

Use of terminology is consistent throughout, for example:

- ☐ 'Primary Investigator' OR 'Chief Investigator'
- ☐ 'Study' OR 'Trial' (we have chosen the former for this document)

The approved protocol will provide sufficient instruction to conduct the study and deliver the intervention.

There are documented processes for managing any deviation from the approved protocol and any required protocol amendments.

Synopsis

Prepared from information in the grant application and includes the:

- Background and Rationale
- Primary Objective or Aim
- Study Design
- Study Arms/Groups (Intervention and Controls)
- Sample Size
- Endpoints or Outcomes

Background and Rationale

This section ssummarises the existing body of knowledge that supports the study. It will include:

- Disease statistics, details of the population affected, existing treatments, gaps in knowledge, etc.
- Referenced evidence (listed at the end of the protocol)
- A rationale for the trial that clearly justifies the need for the study

Aims and Objectives

These should be related to the hypothesis of the study

- The Aim describes the intention of the study, what will be achieved or answered
- The Objectives (usually more than one) describe what the study will do to achieve the Aim
- The Primary Endpoint is a measurement to determine whether the Aim has been achieved: Secondary Endpoints measure other relevant questions asked within the study

Study Design

Describes the type of study, why it is appropriate for the study and:

- Can deliver the stated Aims, Objectives and Endpoints
- Includes measures to avoid or address potential bias, such as randomisation or blinding and whole of practice recruitment (vs individual GPs)
- Including a study schema is recommended (see Perera et al[2])

Study Population

This section describes how participants are identified, by whom and where:

- Participants are clearly defined, including their disease/ condition and key characteristics such as age, gender, etc.
- Inclusion, Exclusion and Withdrawal criteria (if applicable) are clearly described
- Describes the recruitment method/s to be employed, e.g. the use of targeted mailing lists, clinic flyers, which health professionals will be involved, etc.

A PC4 'Coordinators Helpful Hints' on Recruitment is available on our website

The Intervention

Provide sufficient detail of ALL the assessments and procedures to enable the study to be replicated:

- Describe the Groups (or 'Arms') that will be involved clearly stating:
  - The differences between the groups, i.e. the 'Intervention' and 'Control' or 'Comparison' Group/s
  - How the intervention will be administered, and by whom and where
  - A flow chart is recommended showing the routes for all the Groups
- Describe how participants are allocated to the Groups:
  - A clearly described method of randomisation is preferred
  - Alternatively, explain the rationale for a different choice of allocation
- Use a Gantt chart to illustrate the duration of each of the phases of the study:
  - http://www.gantt.com/
- Provide a schedule with clear time points and details of any assessments, tests or visits:
  - Provide a rationale for the choice of time point and assessments
  - Use (and reference) validated measurement tools
  - A table of the sequence and content of assessments and follow-up is recommended

Criteria and procedures for withdrawal from the study are documented

Refer to ICH Guideline for Good Clinical Practice E6(R1) if using any drugs or device and ensure all requirements for use are met, e.g., labelling, handling, accountability, etc.

Recruitment & Enrolment

Recruitment cannot commence until the study has Human Research Ethic Committee (HREC) approval. The sequence of recruitment is patient identification, screening and enrolment. Ensure that:

The Patient Information Sheet is:

- Concise
- Content meets HREC requirements: as a starting point, visit https://hrep.nhmrc.gov.au/toolbox/standardised-forms
- Review by Community Advisory Group members is recommended

These can be arranged by the PC4 Office

The process for obtaining Informed Consent is documented and consistent:

- It must be specific, detailing how participants are approached, when and by whom
- There is a script and training for personnel tasked with approaching potential participants
- There is an opportunity for potential participants to ask questions
- There is a period of time for reflection (approx. 2-3 days) for potential participants between the approach and providing written informed consent

There is secure storage:

- Signed Informed Consent Forms are kept in locked cabinets in locked offices
- Databases with patient information are stored in a password-protected computer

Adverse Events

The National Statement defines 'low risk' research as where 'the only foreseeable risk is one of discomfort': discomfort is defined as 'less serious than harm…which can involve body and/or mind. Discomforts include, for example, minor side effects of medication, the discomforts related to measuring blood pressure, and anxiety induced by an interview.' More information is available at *NHMRC National Statement on Ethical Conduct in Research Involving Humans (1999)*[3].

Most PC4-supported research would be defined as 'low risk', however any untoward event in a study participant, regardless of relatedness to the intervention must be reported:

- Adverse Events (AE) or Serious Adverse Events (SAE) are reported to the Primary Investigator who should determine whether it is related or unrelated to the intervention, and determine the appropriate course of action
- In the unlikely event in a low risk study of a Suspected Unexpected Serious Adverse Reaction (SUSAR) the Investigator must notify the HREC as soon as practical

Develop a Case Report Form and reporting procedures for an Adverse Event, including:

- Description of the AE
- Timing and duration of the AE
- Severity and relatedness of the AE
- Action taken

Emergency procedures for un-blinding (if applicable) are documented

Study Outcomes

This section describes how the outcomes are going to be measured:

- The Endpoints are measurable, and relate to the Aim of the study
- The tools used are validated, and provide consistency of interpretation

Statistics

We recommend this section is provided by a statistician: this role may be provided by a member of the Study Management Team or on a consultancy basis.

Sample size description, including:

- Power calculations, adequate to demonstrate clinical and statistically significant effects
- Expected attrition rates
- Statement of justification
- Level of significance
- Feasibility of recruitment

A Statistical Analysis Plan, including:

- Rules for interim analyses or stopping
- Missing data plan
- Methods for analysing outcomes

Data Management

Appropriate Case Report Forms are available and ALL processes involved in the conduct of the study are documented. Consider what is being collected, why, how it will be used, and what type/format of data collection and storage will be required. You will have:

- Documented procedures and identified time points for data collection, including roles and responsibilities
  A PC4 Delegation Log is available on our website
- Databases with appropriate fields, tables, validation checks and back-up mechanisms
- Quality Assurance procedures for data entry including coding (as per a Data Dictionary) and dealing with missing data
- A mechanism to de-identify participant information, which will be stored separately from identifiable data
- An agreed filing convention to manage version control, e.g.: *Study name – document type – yyyymmdd*
- A process for protocol amendments
- Secure storage and security for all study material
  - Forms are kept in locked cabinets in locked offices
  - Computer databases are password-protected and regularly backed up

A PC4 'Coordinators Helpful Hints' on Data Management is available on our website

Quality Assurance & Control

Quality Assurance (QA) are preventive activities; they are the documents detailing the procedures for data collection and collation during the study to ensure that it is accurate and valid.

Quality Control (QC) are the checks or tests performed to detect errors, such as re-counting, scanning for outliers or checking for consistency (e.g., Title of 'Mr' corresponds to Gender of 'M').

Auditing is a QA activity, a formal, systematic approach completed by qualified individuals that are independent or external to the conduct of the study.

Monitoring is a QC activity, an on-going process of periodic checking or testing usually completed by Study staff.

- QA procedures are documented
- QC time points and activities are identified, i.e. daily, weekly or monthly during data collection, data entry and data cleaning

Budget Management Plan

Budget management is the process by which costs or expenses incurred are formally identified, approved and paid.

- [ ] A budget management plan and responsibilities are documented (or available in a separate document)
  A PC4 Budget Template is available on our website

Dissemination Plan

This section will explain when, how, where and to whom the results of the study will be disseminated

- [ ] Publication plan is prepared, including guidelines for authorship and identification of potential journals
- [ ] Relevance of findings for practice is included
- [ ] Includes a mechanism to provide feedback to interested participants

Data Sharing Plan

As per the requirement by some journals that trials must be registered (i.e. after HREC approval and before recruitment commences) on an appropriate clinical trial registry (e.g., ANZCTR) for submissions to be eligible to be considered for publication, there are varying requirements to include a data sharing plan, which would include:

- [ ] What data will be shared
- [ ] Who will have access
- [ ] Where will it be stored
- [ ] When will it be available
- [ ] How will it be accessed

1 NHMRC National Statement on Ethical Conduct in Research Involving Humans 2007
2 Perera et al; A graphical method for depicting randomised trials of complex interventions, PaT Plot: http://www.cebm.net/index.aspx?o=4200
3. https://www.nhmrc.gov.au/guidelines-publications/e35