



Guidance: Developing a protocol for a clinical research project

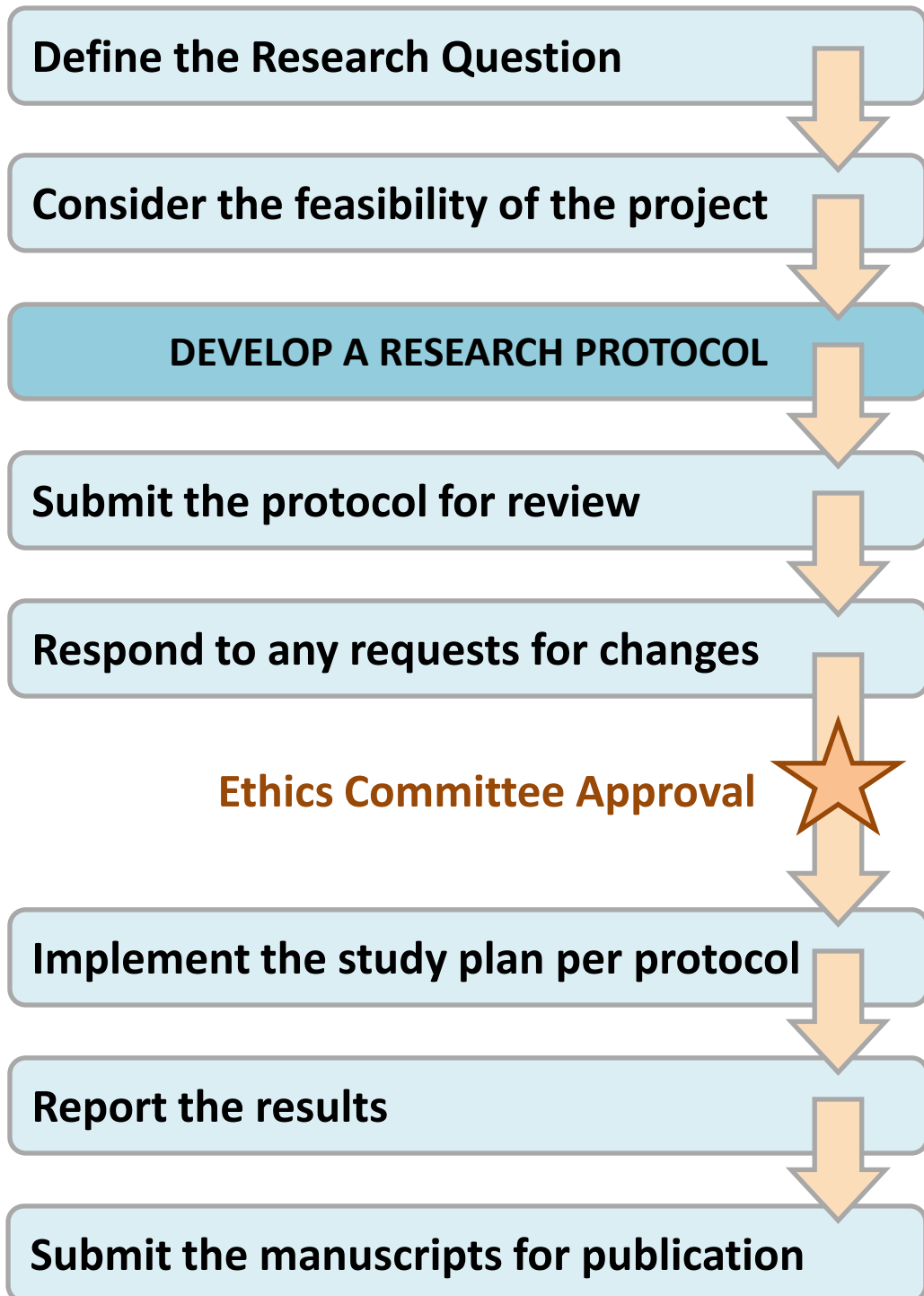
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One must navigate the following process successfully to take a study idea and turn it into a publication that may have an impact on clinical practice or policy:



What is a Protocol?

A research protocol is the document that outlines the study plan for a clinical research project. The study plan must be carefully designed to safeguard the health and safety of the participants, as well to answer specific research questions.

A protocol gives written evidence for the necessity and feasibility of a research study. It provides a full and detailed description of the objectives, design, methodology, statistical considerations and organisation of the study, including specific details on how the research will be conducted and evaluated. The protocol will be followed strictly by the researchers throughout the duration of the study, so the final protocol must be clear and provide enough details for all those involved in the study to use it.

Why is a protocol necessary?

Quality and Publishing

A well written and complete protocol is essential for a high quality study.

Many clinical studies have problems with incompleteness, ambiguity and inconsistency. Many of these problems are avoidable by careful planning during the protocol writing process.

Writing a detailed research protocol will require you to make decision on the aims and objectives of the study, what measurements need to be made, the group of patients to be studied and how the data will be analysed. Time spent on writing a detailed protocol will avoid problems during the study, and will make publishing the results easier.

Approval

Human Research Ethics Committee (HREC) approval will only be granted to studies with an adequate protocol. A complete, detailed protocol allows the HREC and other reviewers to make a judgement about the scientific aspects of the study. It can be used as a reference to answer any questions that are not immediately apparent from the ethics application forms.

A protocol that is considered inadequate will not be approved by the HREC, and queries and/or requests for changes will be addressed to the researcher, requiring a response before the study will be considered for approval again. This process can delay the commencement of the study, and can be avoided by submitting a high quality protocol in the first instance.

Following approval by the HREC, the protocol becomes the legally binding, definitive document for the study conduct, evaluation and reporting. Once a protocol is approved, it is essential that the study is carried out in accordance with the details in the document, as you only have approval to do the research as described in the protocol.

What do I need to do before I start writing?

The first and most essential part of writing a study protocol is to ensure that you have a clearly defined research question. This should clearly define: the population under study, the difference between any groups in the study (for example, the intervention and comparator) and the main outcome(s) that will be measured.

A good study question should be feasible, interesting to the investigator, novel, ethical and relevant. It is important to consider the novelty, feasibility and ethics of the study question early in the development of your study to ensure that the project will succeed. Think ahead about challenges (scientific, regulatory, cultural, and logistical) and consider key questions of feasibility such as:

Is there clinical equipoise regarding this research question?

Are there enough potential subjects to meet your accrual goal?

Are the patients and families to be involved in this study likely to find the study acceptable?

Some of the important steps in developing a research plan include conducting a detailed literature search, building a team of collaborators, writing a draft of your specific aims, doing some initial sample size calculations, drafting a timeline, applying for funding and determining when you will submit an application to the ethics committee.

Statistical issues should be considered at an early stage: how will your data be managed in terms of data collection and storage?; how will the data be analysed?; and will the study have adequate statistical power and/or precision to answer the research question of interest?

Good clinical research makes extensive use of professional statistical advice. In this regard, the Clinical Epidemiology and Biostatistics Unit (CEBU) is funded by the MCRI and University of Melbourne Department of Paediatrics to provide advice and support in research design and analysis to researchers on the Royal Children's Hospital campus.

CEBU strongly encourages researchers to involve CEBU staff in research projects as early as possible in the development of the project (e.g. at the design stage and/or at the time of writing the protocol) to ensure that your study will be able to answer the question of interest. For further information see: www.rch.org.au/CEBU

Writing a clinical protocol is an elaborate, collaborative task that requires the talents of many contributors to ensure a result that is scientifically sound and logistically practicable.

Find suitable people that will be willing to review your study concept and drafts of your protocol. Protocols are often lengthy, complex documents; you will need more than a single review to catch all mistakes. Many eyes make accurate work; review both among and outside of the team can make the difference.

What sections must a protocol contain?

Protocols are always composed of the following three main sections: Background, Aim and Plan of investigation.

These sections generally contain details of the following:

BACKGROUND

- Analysis of previous literature and studies
- Rationale of project

AIM

- Research question
- Objectives

PLAN OF INVESTIGATION

- Study design
- Description of the study population and study groups
- Sequence of procedures
- Variables to be measured and measurements methods
- Planned statistical analyses

However, each protocol is different, and the required content depends completely on the study design and complexity.

Depending on the proposed study, a protocol can be anything from half a dozen to over a hundred pages long. Protocols less than 6 pages long rarely contain all that is required.

How can I get help with protocol writing?

It is a good idea to write an outline of your project, based on the sections listed on the previous page, prior to seeking help, as this will make key details of your project clear.

CRDO

Contact **Julie Smith** at the Clinical Research Development Office (CRDO) for specific advice on what to include in the protocol for your clinical research project, or to have your draft reviewed:

Phone: **9345 4112**

Email: Julie.smith@rch.org.au

CRDO also runs short seminars on protocol development.

Visit the MCRI intranet, or www.rch.org.au/CRDO, for scheduled dates.

CEBU

The Clinical Epidemiology and Biostatistics Unit (CEBU) supports researchers with many aspects of research design, protocol development and statistical analysis. This can take various forms ranging from one-off consultations to on-going collaboration for the life-time of a project. In particular, CEBU will generally provide a trial statistician for any randomised trial that is led by an MCRI or RCH-based investigator (resources permitting).

CEBU also offers courses for staff getting started in clinical research, covering protocol development.

For more information visit www.rch.org.au/CEBU or contact CEBU via:

Phone: **9345 6368**

Email: cebu@mcri.edu.au

Templates

CRDO and CEBU have developed templates to assist in protocol development, annotated with guidance on how to write each section. Approval for a protocol is easier, and the protocol is more likely to be complete if it follows a particular layout or template.

Not all of the sections in a particular template may be relevant for every protocol and the exact form of your protocol will depend on the situation. Therefore you must adapt the protocol template to customise it for your study.

You can download a protocol template from the MCRI intranet, or www.rch.org.au/CRDO