8.5: Developing the proposal

When developing the proposal, it is wise to follow a systematic approach. In Box 8.1, a 10-step chronological, algorithmic approach is summarized that might be helpful for less experienced grant writers.

5.1 What is the problem, and why should it be studied?
The first step is to define clearly the primary research question to be addressed by the trial. Next, articulate why it is important and how the knowledge or evidence derived from the trial will contribute to addressing one or more health problems. Many proposals fail because too many questions are being asked and the proposal is unfocused.

Box 8.1 A 10-step guide to preparing a grant application

1. What is the problem, and why should it be studied?
   ◦ Primary research question
   ◦ Why is it important?
2. What information is already available?
   ◦ Literature review
3. What are the objectives of the research?
   ◦ Purpose of the trial
   ◦ Specific objectives
4. How will the information be collected and analysed?
   ◦ Study design
   ◦ Data collection methods; sampling; data processing
5.2 What information is already available?

A good, but brief, literature review of what has already been done in the research area is an important element of any grant proposal. It demonstrates that the applicant has looked at the relevant publications to identify gaps and opportunities in the field on which the study is based. Wherever possible, past work should be summarized in the form of a systematic review, as discussed in Chapter 3. This stage should also include a review of any relevant registered trials that have not yet been completed.

5.3 What are the objectives of the research?

The title of a proposal is the first thing that the reader sees. After identifying the research question, produce a title that gives the reader a clear idea of what it is hoped to discover. Respect any word limits imposed by the funder.

The next step is to formulate the aims and specific objectives. These vary, according to the nature of the study. For a straightforward trial, for example, comparing the effects of two drugs, it may be relatively simple to state the aim. It may simply be to show whether drug A is superior to drug B in curing a specific disease in an individually randomized controlled trial.

In more complex studies, it may be necessary to articulate a general aim, followed by a list of specific objectives, some of which may include sub-objectives. Sometimes, several sequential steps may need to occur. In vaccine studies, for
example, the immune status of the target population may need to be assessed first to select the target group for vaccination, and, before that, immunological assays may need to be developed, or tested and evaluated in the specific target population for the trial.

5.4 How will relevant information be collected and analysed?

The study design is a major component of a trial. Whether it should be placebo-controlled, double-blind, stratified, cluster randomized, etc. depends on many factors. State why a particular approach is necessary, and, if apparently superior designs have not been chosen, state why not. Many of these issues are discussed in Chapter 4.

The data to be collected and how they will be analysed must be described. If any of the data are to be from a sample of trial participants, the sampling technique needs to be explained and justified. Describe how the data will be processed and what statistical tests will be used in the analysis. Discuss any ethical, legal, and social issues that could arise from the specimen or data collection, storage, and dissemination. For example, it is important to describe informed consent processes for the trial population, what examinations will be performed on participants, and who will be responsible for their health care during the trial. Issues related to the taking, storage, and analysis of biological specimens should be addressed. If there are no previous published data to guide study design, will existing preliminary data or a pilot study be important? These issues are dealt with in detail in other chapters.

5.5 Community engagement plan

The proposal should include a description of how the community will be engaged in the planning and conduct of the trial (see Chapter 9). This should include a brief description of any formal structures, such as a Community Advisory Board (CAB), and other mechanisms that will be used to solicit the trial community’s support and advice and to keep them fully informed of the trial’s progress and results.

5.6 Who will do what and when?

The work plan is important to show in a logical way what aspects of the trial will be done and when. If a trial is ‘high risk’, this should be because the topic being studied is intellectually and conceptually challenging, not because it has been inadequately planned.

For nearly all trials, certain steps need to be conducted first, before others can proceed. A ‘Gantt chart’ is a helpful tool for project planning and presenting the proposed work plan, especially if there are complex dependencies among several components. Gantt charts are used to illustrate a project schedule, indicating in a graphical way start and end dates of specific components and activities to show how the individual tasks are sequenced.

It is important to identify specific milestones in the planning, conduct, and analysis of the trial and if strategic decisions will need to be made and when, such as whether the trial should continue or be stopped, given defined developments or outcomes.

Typical intervention trials involve large teams of people such as recruiters, interviewers, nurses, clinicians, laboratory technicians, public health officials, data management staff, statisticians, collaborators, and consultants. These have to
be carefully managed, and their work budgeted for. In many cases, additional training may be needed. How the trial team will be managed and the work will be coordinated should be summarized in the proposal.

5.7 What are the risks?

In any research undertaking, there is a chance that the objectives will not be achieved because of unexpected changes in circumstances. It is a good strategy to have contingency plans to cover areas where there are such potential risks. While it is impossible to anticipate all risks, list the known ones. Do not wait until reviewers point them out. It shows awareness and preparedness to alter plans without jeopardizing the main aims of the proposal. A good risk management plan would anticipate potential issues and corresponding solutions to prevent delays, increased cost, or poor quality to the study data. An example of a potential, and not uncommon, risk would be that the trial recruitment rate will be slower than anticipated. Potential ways of dealing with this could include close monitoring, so that remedial action can be taken early, using conservative recruitment estimates or planning recruitment at times in the year when the population is most accessible, for example. Contingency plans are particularly important in high-risk research. Identify the potential pitfalls, and describe how plans will change if they arise. For example, what is the alternative strategy if it proved impossible to conduct the trial in one of the trial populations?

5.8 What resources are needed?

Some funding programmes invite proposals that must cost less than a specified amount, and it is necessary to design a study that fits within that budget limit. Whether or not there is a specified budget limit, much thought needs to be given to the budget. On the one hand, an inflated budget could render a proposal uncompetitive if equally strong proposals cost less. On the other hand, an under-budgeted trial may not be completed, and the results will be unpublishable. Be honest about what is needed. Discuss with the officer at the funding agency if guidance is required.

Funding agencies usually provide a list of costs that are eligible to be included in a grant application, i.e. costs that they are prepared to cover. It is important to study the conditions carefully. Salaries must be commensurate with qualifications, fairness, and compatible with local contexts. If equipment is being requested, maintenance costs may need to be factored in. In intervention trials, other costs associated with medical treatment and social care may have to be included. Some agencies do not fund institutional overheads or limit them to a maximum percentage of the total budget, so it will be necessary to check that these are acceptable to the applicant's institution in advance. Institutional contributions could be important to show their commitment to the trial.

Sometimes, it is possible to leverage donations of drugs or supplies from pharmaceutical companies—these can lower the overall costs and make a proposal more cost-effective to funders. If the specific proposal is linked to other projects, provide detail of what is already funded, and be clear about how much funding is being sought and how much will come from other sources. The key message is to cost the trial carefully, and justify all the costs requested.

5.9 How will the project be supervised and administered?

The grant application should demonstrate, for the conduct and analysis of the trial, that the trial team either has all the necessary skills and experience or will have access to the appropriate expertise. This may include aspects of trial...
governance and monitoring of GCP and Good Clinical Laboratory Practice (GCLP) (see Chapters 16 and 17). It may be possible to delegate some of the trial procedures to specialist clinical research organizations (CROs). These units often have specialists in clinical trials to run certain aspects of a trial such as GCP or GCLP monitoring procedures.

Unless the trial is small, it is worth considering setting up a trial steering committee to guide and support the organization and monitoring of trial activities and guide its development, as the trial progresses. The steering committee should include members that represent a broad range of perspectives relevant to trial management. The steering committee also has the task of working with the DSMC to monitor progress and results without compromising the study design, especially in blinded studies (see Chapter 7).

5.10 How will results be disseminated?

The results of intervention trials are generally expected to contribute to the formulation of health policies and practice. It is important to think about how the results of a trial might be used.包括政策制定者和官员在公共卫生部门的早期规划和设计阶段以及在整个试验过程中保持知情，可以加快采用试验结果到政策和实践。资金机构喜欢看到对资金的快速影响，因此在申请中明确这一点可能是一个优势（参见第23章）。

干预试验，由于其本性，通常会产生大量的个人数据和生物样本。样本和数据的存储和访问可能带来复杂的伦理和法律问题。谁拥有样本和数据，谁可以看到个人数据，信息和样本应该如何保存，存储费用如何支付，等等，都是相关问题。资助机构通常要求在试验结束时公开访问数据，并且研究者必须在申请中解释如何管理这一要求，考虑到保密问题。

5.11 How will the application be presented to funding agencies?

Most funding agencies have detailed instructions on the application process available on their Internet sites. Read the instructions carefully, and contact staff at the funding agency if anything is not absolutely clear.

Meeting deadlines is important. Sometimes, funding committees meet only once a year, and, if the deadline is missed, it may be a year before another submission can be made. Do not aim to submit just before the deadline—allow time, and submit ahead of the deadline. Sometimes, funding organizations need clarification if something is not clear in the application. Submitting early allows these issues to be sorted out, before the funding committee meets.

Do pay attention to details. Answer all the questions in the application form. For good presentation, make sure the proposal reads easily, for example, by minimizing the use of abbreviations and acronyms. Avoid technical jargon where unnecessary, and supply clear definitions of any technical terms that must be used. The proposal should be clear and succinct, free of contradiction or ‘leaps of faith’, and readily understood by scientists outside the immediate field of the investigator. Pay careful attention to its structure, ensuring it is logically ordered and argued. The aims and objectives of the proposal should be clearly defined at the start. Most space should be given to study design and methods. Use flow...
diagrams and figures where these will help the reader.

Allow time to go through the form several times. Make sure the final application is free of errors (spelling, typing errors, grammar, etc.), so as not to distract the reader. A carelessly put together application is often interpreted to indicate a careless investigator. It is valuable to have one or more colleagues, who have not been involved in writing the proposal, to review it before submission, as they will often pick up inconsistencies and errors that the investigator has missed simply through being too familiar with the proposal.