Session 1: Aims, Hypotheses, Background/Preliminary Data

I. Grants and Protocols are different

Many people have experience writing a grant, and it is common to think that a protocol is just a mini version of a grant. This perception is not correct. Protocols and grants both involve communicating ideas about your science, but the purpose of sharing the ideas, and the audience receiving the communication, are quite different with protocols than with grants.

Grant vs. Protocol Writing: Goals & Accomplishments

Aspect	Grant	Protocol
Purpose	1) To argue why work should be funded 2) To allow grant reviewer to judge whether scientific approaches are generally likely to be fruitful	1) To create a consistent plan for the investigation to follow 2) To allow IRBs/Regulatory Authorities to determine that the benefits of a project exceed the risks, subjects are participating freely/fairly, and subject safety will be monitored during the trial 3) To allow Regulatory Authorities/IRBs to determine that data will be reliable and meaningful with respect to findings
Focus	1) Focus on rationale and the big picture; a series (complete arc) of experiments that will answer a fundamental question 2) General description of procedures/methods	1) Focus typically on one experiment that subjects will complete (can have several parts); often experiment will address one aim/hypothesis, but sometimes can cover multiple aims/hypotheses. Usually subset of a grant; one, or a few, experiments to address one of the hypotheses 2) Detailed description of procedures/methods
Aims/Hypotheses	Frame the research question; Justify experiments that will be used to answer the question	Frame the research question; Justify the populations that will be recruited and all procedures they will be exposed to (each procedure described must be easily relatable to an aim/hypothesis); define statistical success
Background/Rationale	Emphasized, lengthy, extensive literature review; "Why is it logical and important to do this work?"	Less detailed; sufficient to communicate importance of the work (= benefit); "Why put people at any risk to answer this question?"
Preliminary Data	Shows reviewers that your ideas are on the right track and feasible	Shows reviewers that your ideas are feasible and on the right track
Audience	Highly specialized; jargon/abbreviations used liberally	Diverse: scientific to nonscientific; **needs to be accessibly written**

With protocols, you need to communicate just enough about the scientific rationale to make it clear why the research question is important enough to put people at risk to answer. Excessive emphasis scientific details, typical of grants, risks losing your audience. In contrast, details of the procedures, seldom elaborated in grants, are critical to allow the audience to visualize a subject's experience in the study and to assess the study risks.

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II. Specific Aims – for Protocol Writing

- Should be the answer to the question "What do I want to accomplish in this study?"
- Should be general and deal with the nature of the scientific inquiry ("To understand…," "To investigate…," "To describe…").
- Should be worded identically to those appearing in any grant funding the work (though the protocol often has only one, or a subset, of the corresponding grant aims).

III. Hypotheses – for Protocol Writing

- Should be the answer to the question "What do I think my results will show?" and is the basis for statistical testing (is usually the alternative hypothesis).
- Should be present whenever the goal of research is to make comparisons between conditions or groups. It is generally not good practice to do a study "just to see what happens" (except possibly for very early pilot/feasibility projects). You should usually have an educated guess, based on your background literature review, of what will be seen. It is OK if your hypothesis is refuted by the results (it is best to design studies where if your guess is incorrect, the results provide an equally satisfying answer, or point to an alternative explanation to explore).
- Purely descriptive studies (no comparisons being made) do not require hypotheses; it is sometimes appropriate to construct hypotheses to illustrate a priori thinking about a research question.

IV. Background – for Protocol Writing

- Should **not** be a focal point of the document (like it is in a grant)
- Should **not** be copied and pasted out of a grant; this will be too complex for the protocol audience. If the protocol reviewers can't follow the importance of what you are doing or how you are doing it, it will not be approved.
- Should be ~ 1-3 pages total – enough to achieve the objective: communicate that this has not been studied before and why it is worth putting people at risk to obtain this knowledge.
- Should cite key publications, especially in the areas closest to the current research question; exhaustive literature review is needed to design your protocol, but referencing all of these studies in the protocol is not needed.
    - Advice on literature review. Like research itself, this is another area where much is assumed about our abilities because of having gone through medical sciences education. But even people who are experienced in literature review can stand to hone their skills. The librarians at the UCD Health Sciences Library are outstanding resources for this topic. They will provide consults on a specific literature review. Sign up for a consult by clicking on the "Ask Us" tab on the right side of the HSC Library home page. Plan on 1-2 weeks out to schedule your consult.
- Should justify your study design. This idea is particularly relevant in the following circumstances:
    - If you are proposing any kind of medical care intervention and randomizing to different treatment arms, you must communicate why there is clinical equipoise between these arms (i.e., there should be sufficient information to support why any of the treatment options can be acceptable care).
    - If you are proposing a particularly risk study procedure (e.g., invasive sampling procedure), your background should communicate why such a risky procedure is necessary. For example, if you need to perform a liver biopsy to examine histology, your background should address the outcomes needed to answer the question, why liver histology is critical, and why alternative and less invasive measures are inadequate.

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- Should be organized in three general sections, as described below. **Start by first writing a concise, 1-2 sentence answer to each of these sections' questions.** In addition to being concise, really try to communicate just the critical components of your ideas in these three answers.
    - Section 1: Why is it important to study this problem?
    - Section 2: What is known about this problem, and what is/are the important gap(s) in knowledge that need(s) to be addressed?
    - Section 3: How will the current study address these gaps?
- From these initial statements, develop each section as described below. You should start broad and *quickly* narrow focus. Here is a suggested approach to try to follow. This is a general guide, and it is difficult to write a guide that will fit all studies. More complex studies might require more background; you can use more sentences/paragraphs than this guide advises, but understand that the more you write, often the less clear and effective it is to achieve its objective. Brief and to the point is often beneficial:

Section 1 (1 paragraph)

- Why is the general field of study important to humans (1-2 sentences)
  → Who is affected by this problem (identifies who will be the subjects in your study, or at least who will ultimately benefit from the work), if this not already apparent above (1-2 sentences)
    → why focus on this particular sub-area of the problem (1-2 sentences)
      → why focus on this particular sub-sub-area of the problem, etc. (1-2 sentences) – this subsection may need to be repeated to get down to the level at which you are asking the question

Section 2 (1-6 paragraphs, depending on complexity of the problem)

- What is currently already known about this sub-sub area, as it relates to what you are studying (½- 2 paragraphs)
- What is currently done to remedy the problem being studied (½- 2 paragraphs)
- **What gaps are there in the current knowledge, or remedy approach to the problem, that are in need of filling** (½- 1 paragraph); the "gap" or "unmet need" explanation is critical to justifying your work. Do not forget to include a clear statement about this gap/need; it is not as obvious to your audience as it is to you.

Section 3 (1 paragraph)

Final paragraph (a.k.a., the "key paragraph") should provide a neatly-tied bow of why this study is therefore being conducted. It should be a logical conclusion of what was described above, in terms of this being the next logical step in furthering the field of study. It should be clear that this question has not yet been answered, and why the answer is important and will impact medicine.

V. Preliminary Data – for Protocol Writing

- Should briefly describe unpublished data you have generated in working toward answering this question. The objective of this section is to communicate 1) "We have already conducted similar work in this area, which is why we will be able to complete this study" and 2) "Look at what we have already learned, which is why this study is

promising." Make sure everything you include communicates one of these two themes; even use this wording to make it obvious why you are including the information.

- Again, this should be brief and to the point, with strong topic sentences in each paragraph that tell the reader which of the two points above you are illustrating in each paragraph.
- Figures are helpful in this section (a picture is worth a thousand words).
    - Note that published studies will likely be included in your background section; they have already added to the body of literature. The data presented here might be unpublished pilot data obtained under previous IRB-approved protocols, or unpublished non-human data presented at a conference.
- It is OK to indicate that there are no preliminary data. However, if this study requires specialized procedures or analysis, it will be important to somehow communicate your ability to do these procedures competently. Showing some graphs of data illustrating your lab techniques, for example, would be helpful.
    - If all you have is previously published studies, and no new unpublished data, it is still worth stating in this section that your group has experience in each of the techniques that will be used in this protocol, whether that is recruiting this particular subject population, conducting the data collection procedures, or specific analysis/assay methods that are key to this study. Each of these statements can cite studies that are included in the background, and you can show a figure or two to illustrate either of the two key points.