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Tips for Successful Written Preliminary Exam Proposals

1. **You are not writing a research proposal.** You are writing an exam in the format of a research proposal. If this were a real grant application, then students could get more help (e.g. feedback on writing). Furthermore, the exam is evaluated on a very different basis than a grant application, starting with anonymity and not considering the qualifications or experience of the author, as well as no limit on the number of proposals that can be successful. We chose the format of a research proposal because it provides a good opportunity for students to demonstrate their thinking skills, so be sure to do so. For example, in a real grant application reviewed by experts, the author could cite a well-known reference in the field and move on. For the exam, you need to explicitly explain your reasoning at every step.

2. **Use what you learned in MCRO795.** You have taken a semester long class in creating and writing research proposals. Do not ignore what you have learned from that experience. When considering potential topics, write a Specific Aims page using the template from class. If you cannot write a satisfactory Specific Aims page, then you probably have not chosen a suitable topic for your proposal. For the full proposal, use the MCRO795 templates at least as a starting point to be sure you have everything you need down on paper. If you find a better way to organize or communicate your ideas, then you can rearrange things with the confidence that all the important parts are present.

3. **Resources available on MCRO795 Canvas site.** You still have access to the MCRO795 Canvas site, which contains multiple documents from the course that are useful for preparing research proposals, including templates and advice for different sections of a proposal, samples of successful proposals, a summary of key lessons from MCRO795, etc. In addition, there is a Written Prelim Resources folder with guidelines, tips, sample prelims, etc. Based on comments from the course evaluation, it appears that some students were not aware of all the resources in the Templates & Examples folder, so that might be worth another look.

4. **Use your time wisely.** There are two behaviors closely associated with bad outcomes on the written prelim. The first is procrastination. Writing a good proposal will take much longer than you think. Choose your foundation paper and proposal topic by February 1, which will give you six weeks to create a draft Specific Aims page with which you are satisfied by the March 11 deadline. If you don't start writing seriously until the May protected writing period, then do not attempt to do any lab work at all during the writing period.

   <u>The task of creating and writing an original research proposal can seem overwhelming the first time that you do it, so make an explicit plan.</u> Break the task into smaller pieces of whatever size makes you comfortable (e.g., choosing a foundation paper, reading a certain number of background papers, talking to a certain number of people, outlining various pieces of the proposal, completing the first draft of various pieces of the proposal) and set yourself deadlines for completing

each task. After identifying all the steps, work backwards from your planned submission date to see how much time is available for each. Build in some slack time for unexpected challenges.

Establish ways to force yourself to stick to your schedule. This typically involves engaging with others. For example: (i) Share your plan with a friend, partner, fellow student or even your advisor and ask them to check on you weekly. (ii) Schedule meetings with others to discuss aspects of your proposal. This can be done well in advance, before you are even ready to talk. The deadline of an impending meeting will force you to prepare, which keeps you on schedule. (iii) Regularly scheduled writing groups, where students working on the exam get together in the same room (or even on Zoom) to just write.

Work on the exam should not expand to fill all available time, which would just make you miserable. A proposal does not need to be perfect to Pass. Students are given a five-month period to work on the exam to provide maximum flexibility, not because we expect the exam to take that long. Before draft Specific Aims pages were required, one student did their entire proposal in the 3.5 week protected writing period and passed. We strongly discourage procrastination but share this anecdote to point out that the exam should not take anywhere near all of your time for five months.

5. **Talk with others about your ideas.** The second behavior associated with poor prelim performance is isolation. Students who disappear during the exam period tend to do poorly. Get out and talk to people about your ideas. Send email messages to the leading researchers in the field of your topic and ask them for the latest unpublished news. They will be pleased that you asked, and probably would like to receive a copy of your final proposal. Although it is very beneficial to talk to others, remember that this is your proposal, and you will need to take the lead in thinking and developing your ideas. You cannot expect everything to fall out of conversations. Some ideas about talking with others:
   - It is important to discuss the foundation paper with someone who has read it to verify that you correctly understand the foundation paper. Also, this is an easy way to start talking with others because the first conversation can be simply about the paper and does not need to include your original ideas.
   - You don't know what you don't know. You can think everything about your proposal is fine, but if you do not talk to others about your ideas then you won't know if you have overlooked something that could be critically important.
   - All students had research experiences before coming to UNC. You may have a good relationship with a former PI as a senior person with whom you could talk. Senior personnel have the experience to be especially useful in assessing "Big Picture" aspects of research proposals.
   - The first author of your foundation paper may have more time (and seem less intimidating) than the senior author. Talking to the first author early in the exam process is a good way to identify what follow up questions are viable and considered significant by the field.
   - Remember that every person in the Prelim Consulting Corps or the Peer Mentor Network volunteered to talk with students taking the exam. You should feel no

barrier to approaching people in the PCC/PMN. Indeed, it would be stunning if anyone in the entire Microbiology & Immunology department (other than faculty, who are prohibited) declined to talk to you about your ideas when asked.

- A past student set a goal of talking to 8 to 10 people about their ideas. In addition to the benefits of conversation, preparing for the meetings helped clarify their thinking.
- Past students rounded up people from nearby labs for a joint discussion or took over a group meeting without the advisor present. Group dynamics were helpful. When one person had a point to make, others could build on it in a collaborative manner. The result was a more coherent outcome and faster progress than if the student had to go off on their own and track down information.
- A past student adopted a multi-pronged approach - speaking with the first author of the foundation paper, who was very valuable in sorting out what was known or not known in the field; meeting with their full lab twice; and also meeting with individuals.
- To preserve anonymity of grading, it would be prudent to tell anyone that you speak with from UNC to please keep your proposal confidential. The goal is to avoid someone having a conversation that inadvertently discloses your topic to UNC MCRO faculty members.

6. **Advice from senior MCRO students.** Although most of your discussions about prelims will be about the science, it will be helpful initially to talk with MCRO students who have passed prelims to get their ideas about the best strategies and tactics for approaching the task. We intentionally start this process with a student panel at the orientation meetings. It is particularly important that students in labs without any senior graduate students seek out senior students in other labs for some initial advice. Senior MCRO students (and their contact information) are included in the Prelim Consulting Corps. If conversations lead to any questions about what is or is not allowed, be sure to ask the Prelim Exam Advisor [Bob Bourret, bourret@med.unc.edu, 919-215-2733 (cell), 6108 Marsico Hall] for clarification.

7. **When, what, and how to talk about your proposal.** Just as we advocate rewriting a Specific Aims page multiple times to get the logic of the whole project worked out before writing most of a proposal, it is wise to talk with others early in the process about the topic and logic of your proposal. This will help you figure out your ideas before you get too far into your plan, even before you write your draft Specific Aims page. In other words, it can be very helpful to talk to others about the "Big Picture" ideas for your project, and not just about the experimental details of your approach.

   When seeking feedback on the overall topic and scope of your proposal, do not be shy about talking to senior people, who have more experience with this aspect of planning scientific projects than graduate students. Other tactics to increase the value of a conversation include convincing someone to read the foundation paper and discuss it with you (which has the added benefit of ensuring that you fully understand the paper), or a group discussion/brainstorming session, which will have different dynamics than a one-on-one conversation. In either case, be sure to exclude other students using the same foundation paper as you for their prelim.

Remember the central rules about prelim advice: To a first approximation, (i) you can talk to anyone about any aspect of your proposal except you cannot talk with Microbiology & Immunology faculty members and (ii) you cannot show anyone except UNC Writing Center coaches any text that will end up in your proposal other than the Specific Aims/sub-Aims themselves.

8. **(Hopefully not) dealing with the pandemic.** In the unlikely event that pandemic conditions, which are inherently isolating, return then some specific strategies to consider include:
   - If you are someone who uses your physical location to provide cues about work/life balance and find it difficult to work at home, then be sure to find a location outside of home where you can focus on your exam. It is unlikely that campus will entirely shut down again as we did in 2020. One option is that campus libraries have private study rooms that you can reserve.
   - It can be difficult to talk about your ideas without the ability to draw, and the Zoom whiteboard function is awkward. There are many workarounds. There are inexpensive apps that can connect your smartphone camera to your computer so you can share the image of live drawings. You can buy a USB connected webcam from Amazon for ~$35 for the same purpose. Instead of an extra camera, you can buy a USB connected drawing tablet that uses a stylus from Amazon for ~$40 for a 4"x6" screen and ~$60 for a 6"x10" screen. Any of these devices may be useful outside of your exam. If you do not want to buy one for yourself, consider asking your advisor to buy one for your lab.
   - Limited time on campus can seem to impose a barrier to spontaneous conversations about your ideas. Students sometime feel like they must accumulate a lot of questions to justify setting up a Zoom call. Do not make excuses to avoid conversations. Some students found texting to be an informal way to have a brief conversation. The Peer Mentoring Network may have open office hours where you can talk without an appointment.

9. **Choosing a topic.** Although the foundation papers substantially constrain possible choices of proposal topics, students typically find that choosing a topic and scope of investigation that faculty reviewers judge to be acceptable is the hardest part of the exam. Some things to keep in mind include:
   - You have two general options – follow up foundation paper or apply foundation paper to something else. If you don't like any of the foundation papers, then figure out how to bring one of them to something of interest to you. There is no point in being miserable for the semester working on a topic that does not interest you. The connection between foundation paper and the final proposal must be plausible, but can be pretty distant.
   - One of the biggest criticisms of the MCRO prelim exam format as a non-dissertation research proposal is the perception it is a missed opportunity to advance your dissertation research. You can intentionally frame your proposal to capture some of the effort spent on the exam for the direct benefit of your dissertation research. For example, your prelim proposal could incorporate

methods that you want to use in your dissertation research. However, be sure that the methods match the questions.

- Use citations in paper itself and Scopus/Google Scholar to track down what has been published on your topic, e.g. who has cited your foundation paper. Another resource is www.connectedpaper.com, which attempts to identify related papers that do not necessarily cite one another based on citing or being cited by the same sources.
- Note that Google Scholar searches the entire content of papers, not just titles and abstracts like PubMed. This can help locate otherwise obscure information, e.g. what is known about a specific residue number in a particular protein.
- Commentaries on foundation papers might be a source of ideas for new or unanswered questions.
- Grant abstracts from the foundation paper authors in NIH RePORTER could be a source of project ideas.
- Avoid topics where only one or a few papers have been published, even if the topic is really cool. You need something where the initial descriptive work has been done and enough is known to allow formulation of models or hypotheses. It is difficult to write a successful discovery science prelim proposal. Foundation papers are intentionally chosen to avoid the problem of too little information, but lack of basic knowledge about a topic may be relevant if you jump off in a different direction than simply extending the foundation paper.
- You want to be able to ask questions about "How does it work?" rather than "What happens if…."
- Remember the two papers we read at the start of MCRO795:
  Alon, U. (2009) How to choose a good scientific problem. *Mol. Cell* **35,** 726.
  Casadevall, A. & Fang, F.C. (2009) Important science - It's all about the SPIN. *Infect. Immun.* **77,** 4177.

10. **Topic "do's':**
    - Recognize that basing a proposal on a foundation paper is different for preliminary examinations than it was for MCRO795. In MCRO795, one focus was the mechanics of proposal writing, which can be practiced even with a suboptimal idea. In contrast, your ideas really matter for the preliminary exam.
    - A Specific Aim should encompass a sufficiently large and logically coherent collection of experiments that it would result in at least one publishable paper if successfully completed. A paper in an American Society for Microbiology journal (e.g. *Journal of Bacteriology, Journal of Virology*) is a reasonable standard. A proposal potentially leading to multiple *Cell/Nature/Science* papers is probably too ambitious for the prelim exam.
    - The proposed experiments should be about three person-years worth of work. Proposing experiments that will be entirely completed in weeks or months is too little; something that will take more than three years is too much.
    - A good hypothesis should aim to advance scientific knowledge in a significant way. A simple extension of the line of investigation in a foundation paper is worth considering but may not always meet this standard.

- Testing your hypothesis should allow you to demonstrate your ability to understand and think about an area of research.

11. **Topic "don’ts".** Topics that faculty reviewers will generally judge to be unacceptable include:
    - Simply repeating what was done in the foundation paper in a different organism or cell type generally is not a good idea, because it does not provide you with an opportunity to showcase your ideas/critical thinking and is unlikely to significantly advance the field. It is conceivable that repeating an investigation in a different organism could be considered in unusual circumstances if soundly justified, but if you are not sure, then do not do it.
    - Discovery science/screens (aka "fishing expeditions") can be an important and appropriate research strategy, but rarely make for good research proposals and are particularly poor choices for the preliminary examination. For example, it is risky to propose: "I hypothesize that virulence factor X interacts with a host protein, so I will perform yeast two-hybrid screens to find the interacting partner." The problem is that you cannot be sure what you will find or even if you will find anything at all. Uncertainty about the outcome of a screen makes it difficult to clearly articulate a logical subsequent course of action, so such proposals usually become a generic discussion of the screening technique rather than a thoughtful exploration of the concepts within a field. In contrast, proposals based on testing hypotheses (i.e. hypothesis-driven) allow you to showcase your critical thinking skills.

      Including a screen as a small part of a proposal can be successful, particularly if you can rationally justify at least one candidate to test in addition to whatever your screen finds. Having candidates in hand means that you have something reasonable to do even if your screen completely fails.
    - Avoid proposing to simply fill a technical gap in the literature. For example, if the foundation paper shows that treatment with a T cell depleting antibody protects from immune disease, do not propose to determine if T cell receptor knockout mice have the same protection. This type of work will not significantly advance the field.

12. **Grading criteria.** As you develop your proposal, be sure that you clearly address the five criteria upon which it will be graded.

    - Is there a clearly presented hypothesis or hypotheses? Is the hypothesis supported by a reasonable rationale? Does testing the hypothesis have the potential to significantly advance the field?
    - Are the proposed experiments logically consistent with the Specific Aims, i.e. can the planned experiments actually answer the questions posed? Do the planned experiments represent a reasonable way to address the Aims, or have much better approaches been overlooked?
    - Are the reasons for various choices in experimental design explained and alternate experimental approaches proposed? The nature and extent of what constitutes an appropriate alternate approach depends on the suitability and feasibility of the primary approach.

- Are various possible experimental outcomes and interpretations considered, including the possibility that a hypothesis might be incorrect?
- Is the proposal clearly written and illustrated?

13. **Good Specific Aims.** Typically, a good Specific Aim would be to test a hypothesis or answer a question about how the world works. "We will make an antibody to protein X" is not a Specific Aim. Because the Specific Aims are central to the entire proposal, it is to your advantage to be satisfied with the wording of your Aims, and indeed the entire content of your Specific Aims page, before you start seriously writing the remainder of the proposal.

14. **Independent Specific Aims.** Do not make one Specific Aim dependent on a particular outcome for an Aim that comes before it. Here's a simple example:

    Aim 1. Determine if protein X on the surface of a bacterium is the adhesin for adherence to host cells.

    Aim 2. Identify the receptor on the eukaryotic host cell for binding of protein X.

    In this case, Aim 2 can be pursued only if the answer to Aim 1 is that Protein X is indeed the adhesin. If Protein X is not the adhesin, then there is nothing to study in Aim 2. You can sometimes get around the problem of dependent Aims by rephrasing the goal or the question that is being addressed. In this example, an independent Aim 2 could be:

    Aim 2. Identify the receptor for binding of the bacterium to host cells.

    The revised Aim 2 could be addressed experimentally, even if it turns out that Protein X is not the adhesin. (Note that neither sample Aim is very substantial.)

    If your project necessarily has dependent parts, this can sometimes be handled by grouping the dependent parts together within a single Aim (i.e. having dependent sub-Aims). However, be sure that if an Aim is risky, there are enough other robust Aims to constitute a successful project if the risky Aim fails.

15. **Number of Specific Aims.** Your proposal should have two or three Specific Aims. One Specific Aim is insufficient, because it makes the whole proposal dependent upon the success of that Aim. The limits on project scope (three person-years) and proposal length generally make it unrealistic to propose or satisfactorily describe four or more Specific Aims.

16. **Logical consistency between Aims and experiments.** One of the most common (and potentially lethal) weaknesses in prelim proposals is that the experiments described in a proposal do not relate directly to the question that is supposedly being asked. You may describe a perfectly fine series of experiments, but you will be criticized if the experiments will not reach the goal stated in your Specific Aim. After you have written the experimental plan for each Specific Aim, read through your plan to make sure that the experiments will answer the stated question. Remember the "To… we will…" formulation from MCRO795 to check for logical consistency. Another useful test is to consider what potential results might arise from your

experiments and what you could actually conclude if you obtained such data. If you cannot think of technically feasible experiments to achieve your Specific Aim, then you can always revise the Aim to match your experimental plan.

17. **Do not give the appearance of being "wedded to your hypothesis".** Be sure to consider the possibility that your hypothesis is wrong, and the world does not work the way you think it does. Avoid saying you will prove or establish your hypothesis to be true; what you really want to do is test whether or not your hypothesis is true.

18. **Suitable background information.** Just as you are expected to think critically about your own experiments and how they could lead you astray, your review of relevant knowns should critically evaluate which information has been firmly established and what is open to alternative interpretation.

19. **Explain "why".** Never leave anything to the imagination of your reviewer! One of the most common problems in real grant proposals, as well as in prelim proposals, is that the rationale or overall strategy for a project is not adequately explained. Another frequent omission is that the author does not explain **why** the project is worth doing, and how the information that will come from the proposed experiments will contribute to our understanding of something important or lead to useful things. It may seem self-evident to you why the area you have chosen is worthy of investigation, but there is a good chance that it will not be clear to your reader unless you state your reasoning explicitly. Also, for individual Aims or experiments within an Aim, be sure to explain why you think each is important to do and what you will learn. In a research proposal, explaining why you plan to do something is at least as important is explaining what you plan to do or how you plan to do it. Explain the "why" part near the beginning of each passage. Important explanations or justifications for the overall project or for each specific part of it should not be buried in the middle of densely written paragraphs; such organization almost guarantees that a reviewer will miss at least some explanations.

20. **Use customized subheadings to guide the reader.** As you saw in MCRO795, bold font subheadings are an effective communications strategy. Take advantage of this technique to guide the reader. There is one MCRO795 handout with tips about subheadings and another with examples of customized subheadings in the Specific Aims page, in Significance & Innovation, and in Approach. Also, you can double check the logical flow of your proposal by just reading your subheadings.

21. **Know your audience.** Your primary and secondary reviewers will be in the general field of your proposal. However, because Common Reviewers read proposals from bacteriology, immunology, and virology, there is a two-thirds chance that your Common Reviewer will be out of field. All your readers should be able to understand your proposal.

22. **Careful experimental design & alternative approaches.** Recognize that one experiment can answer two questions by using two outputs. For example, during a time course of an infection *in vivo*, you could study histology samples for tissue

damage and also quantify pathogen burdens. Try separating these two outputs into two subsections to be discussed one at a time, rather than lumping all the interpretation into one big block.

For each of your important experiments, spend some time thinking about what could go wrong with your plan. How might the experiment fail? Remember the false positive/false negative questions from MCRO795: “If I get the expected results, then how could I get them even if the hypothesis is NOT true? If I DON’T get the expected results, then how could that happen and the hypothesis still be true?” Tinker with your methods and controls to address any problems revealed by these questions. If you think the primary strategy is really good and likely to work, then alternative methods do not have to be presented in much detail. If the primary strategy is risky, however, it becomes more important to show the reviewer that you have thought about how to accomplish your goal even if your clever idea does not work out. It is OK to include some risky approaches, if you indicate that you are aware of the potential problems and have some alternatives in mind. If there are some unavoidable potential pitfalls in your experiments, then it is much better for you to point out the problems than for you to say nothing and hope the reviewer does not notice. The best way to defuse criticism from your reviewer is to make the criticism yourself when necessary.

23. **Meaningful details.** Remember to focus on meaningful details when describing your experimental approach. Your faculty reviewers are likely to be familiar with most techniques that you plan to use, and don't need extensive details. By focusing on meaningful details, you will both convey your understanding of the technique to the reader and make space for more important stuff (such as "why").

    It is not sufficient to simply say that you are going to follow a previously published approach and cite a literature reference. The literature citation proves that the method is feasible (good), but it does not demonstrate that you understand the method, which is a point of the exam.

    We don't care if you can regurgitate methods for standard techniques. We don't care how many micrograms of RNA you will use, that you know where to buy qPCR reagents, nor whether you know to add DNase prior to your qPCR reaction. We care whether you can think analytically.

24. **Be realistic about experimental constraints and safety issues.** One of the fun things about the prelim exam is that you do not have to worry about how difficult or expensive it might be to do a particular project. If it makes scientific sense and you show that you're aware of the issues, you can do anything you want! However, you must be realistic in dealing with animals, humans, BSL4 containment, highly toxic chemicals, etc. Be sure to think through what would actually be required to do the work in such circumstances and how your experimental design might be impacted. For example, a typical way to knock out genes when making a mutant is to introduce an antibiotic resistance marker, but you would never be allowed to do this with a BSL4 bacterium. Therefore, your experimental plan would have to include realistic strategies for making desired mutants without using antibiotic resistance markers. How will you safely handle dangerous materials? Animal and human experiments

require acknowledgement that you will obtain permission from the appropriate institutional review boards and follow standard guidelines.

25. **Collaborations**. You can assume you have access to real core facilities and you can establish hypothetical collaborations with real people to provide necessary materials or expertise.

26. **Interpretation of results & statistics.** An important part of the presentation of each series of experiments is to tell what results you might expect, how you would interpret the different possible outcomes, and how those outcomes will influence what you do next. If you will generate some kind of quantitative data (e.g. number of vaccinated vs. unvaccinated mice that die from a viral infection), include a brief description of the type of statistical analysis you will use to analyze the data, and indicate how much difference you would have to observe between the two groups to make a statistically significant conclusion (e.g. that the vaccine provided protection). You do not have to specify statistics software.

    If you plan to use animals or human subjects, then you should include power calculations to determine the sample sizes necessary to obtain statistically valid results.

27. **Your draft Specific Aims pages, part 1.** Do not use the fact that you will get faculty feedback on your draft Specific Aims pages as an excuse to avoid the hard work of thinking about your project and writing your Aims pages. Each draft Specific Aims page should be the best that you can create, so you obtain faculty insight into aspects you do not know how to handle (or even realize that they exist). If you do not put forth your best effort on the Aims pages, then you risk a missed opportunity in which faculty feedback simply addresses issues you already know about or how to resolve, instead of the things with which you actually need help.

28. **Your draft Specific Aims pages, part 2.** A Specific Aims page typically contains just a hint of your planned experimental strategy because you have the whole Approach section to explain everything to the readers. For the preliminary exam, it can be useful to provide more experimental outline in the first draft of the Specific Aims page than will be in the final version so the faculty reviewer can understand and provide feedback on your proposed approach.

29. **Your draft Specific Aims pages, part 3.** The proposal development strategy recommended in MCRO795 is to first think through your project by writing and revising your Specific Aims page multiple times until you are satisfied with the logic and scope of your project, before writing the full proposal. Thinking is generally harder than writing. Because the Specific Aims page captures the essence of your thinking and your project, you will have two opportunities to get faculty feedback on your draft Specific Aims page. The criteria below are provided to faculty to guide their feedback on your draft Specific Aims page and should also be familiar as prompts for descriptive evaluations in MCRO795. You can use the same criteria to double-check your project design throughout the entire exam process.

Foundation Paper

- Is there a clear connection between the foundation paper and the proposal? Does the paper inspire, lead to, act as the fundamental reference for, etc. the proposal? Historically, about half of prelim proposals are direct extensions of the foundation paper and about half apply some aspect of the foundation paper to another question.
- Does the student correctly interpret the foundation paper?

Hypotheses

- Is there a clearly presented hypothesis or hypotheses?
- Are the things claimed to be hypotheses actually hypotheses (informed speculation about how the world works), or are they experimental predictions (if I do X, then I will observe Y)?
- Are the hypotheses supported by reasonable rationales?
- Does testing the hypothesis have the potential to significantly advance the field?

Specific Aims

- Are the Specific Aims hypothesis driven, or do they represent discovery science or technology development? It can be reasonable for a student to include a discovery science sub-Aim, but successful preliminary examinations are primarily hypothesis-driven.
- Are the Specific Aims designed to test a hypothesis or answer a question, rather than simply perform a particular experiment?
- Are the Specific Aims independent of one another?
- Is each Specific Aim of appropriate scope? Successful completion of one Aim should generate results sufficient for publication of at least one paper in a reasonable journal (e.g. *J Bacteriol, J Virol*).
- Are there two or three Specific Aims? The students were informed that one Aim is too few to be viable and four is too many to explain within the page limits.

Significance

- Will the student be able to make a reasonable argument for the significance of their proposed project (assuming that their Aims are achieved)?

Experimental Approach

The draft Specific Aims page will likely contain only limited information about the experimental approach. Based on what you can tell:

- Do the proposed experiments probe causation or are they merely looking for correlations?
- Are the proposed experiments logically consistent with the Specific Aims, i.e. can the planned experiments actually answer the questions posed?
- Do the planned experiments represent a reasonable way to address the Aims, or have much better approaches been overlooked?
- Are the proposed experiments technically feasible?

- Is the overall project of reasonable scope? The guideline is one person working for three years, with unlimited budget, access to core facilities, and commercial support (e.g. DNA sequencing, antibody preparation, mouse breeding, etc.). There is substantial latitude in estimating the needed time, but the proposed project should be more than a few months of work alone and less than two people working full time for three years.
- If the hypothesis is proven false, then would/could there still be a viable project?

Preparation

- Does the draft Specific Aims page appear to be logically complete and well thought out?
- Is the Specific Aims page clearly written?

30. **Your draft Specific Aims pages, part 4.** If you have questions about the faculty feedback you receive on your draft Specific Aims pages or your full proposal, then don't be afraid to ask Bob for clarification.

31. **Use sample prelims with care.** Sample prelims are intended to convey a sense of what constitutes a Passing proposal. Sample prelims are not intended as templates to be closely followed, because student prelims generally contain numerous flaws. Other problems from closely following sample prelims include blindly propagating uninformative subheadings (e.g. Anticipated Results, Potential Pitfalls, and Alternative Approaches) or suboptimal formats for data interpretation (e.g. "If our hypothesis is correct, then we expect to observe…", which puts the conclusion before the data). Samples of funded NIH grant applications (from MCRO795 or your lab) would be better guides to success, but even then you will need to think for yourself about how to write your proposal and recognize that grant applications are evaluated differently than preliminary exams.

32. **Recognize the challenges of writing alone.** The preliminary exam is an unusual writing task because nobody else (other than UNC Writing Center coaches) can read and comment on your proposal. After a while, you will get to the point where you cannot really see the flaws in the proposal, because you are so immersed in it. One strategy is to try to allow time for the proposal to "cool off" for a while before you do your final edit and turn in the exam. Plan your time to get a complete draft at least a week and a half before the final deadline and then do something to get your mind completely off the proposal (e.g. a trip to the beach or mountains) for a few days. When you look at the proposal again, you will be able to see errors and flaws that were previously invisible to you. Alternatively, reading your proposal out loud can help you identify mistakes such as missing words.

    Another strategy is to utilize the Writing Center. The writing coaches can help assess clarity even without understanding the subject. It is important to be able to write clearly for a non-expert audience and there is a 2/3 chance your Common Reviewer will be out of field. If you plan to use the Writing Center, then be aware that they may not be available when you want their input. In particular, the Writing Center may not be open between semesters or summer sessions.

33. **Proof read!** This is important. Lots of typographical and grammatical errors, incomplete sentences, etc. in a proposal annoy reviewers faster than anything else because sloppy errors suggest that you do not care about your work. If you do not care, then why should your reviewer? Once a reviewer gets irritated, then he or she is much more likely to make a big deal about any deficiencies in your proposal. Proof reading is an easy thing to do that makes a big difference in how your proposal will be received. Although not foolproof, the Microsoft Word spelling and grammar tool can help point out many potential problems.

34. **Avoid dangerous words.** Recall the dangerous word list from MCRO795 (Week 03). Be careful about “and” vs. “or” when describing experimental conditions. Avoid ambiguous words such as "these", "those", "this", "its", etc. Say explicitly what you mean and do not worry about being repetitive in the process. Clarity is critical. Choose your words carefully - don't use absolutes such as "all", "never", "identical", “unique”, etc. unless you really mean it.

35. **Create a page layout that is easy to read.** You want to make it easy and enjoyable for the reviewer to read your proposal. Nothing horrifies a reviewer so much (or puts him/her to sleep so quickly) as page after page of solid text, with long paragraphs to wade through. Possible solutions include:
    - Use spacing between paragraphs or sections to set them off from each other. Don’t push the page limits! It’s better to edit down your beautiful prose rather than eliminate space between sections and paragraphs. Minimum font and margin sizes are defined in the formatting rules. Microsoft Word paragraph formatting commands allow you to specify space between paragraphs – it does not have to be a whole line.
    - Use section headings to break up the text and guide the reader.
    - Break things up with figures or tables. Figures do not have to be elegant - this is not an exam that measures your ability to use drawing software. If you choose to modify a published figure, be sure to cite the original source.
    - Judicious use of bold, italic, underline, or colored fonts to draw attention to particularly important sentences.
    - Be sure that the most important sentences are not buried in the middle of paragraphs, where even format highlighting can't save them. Instead, split up large paragraphs.

36. **Active voice.** Active voice is more effective and usually requires fewer words than passive voice. For example, write “Protein X is the adhesin…” rather than “It was determined that Protein X is the adhesin…” There used to be an unwritten rule that it was not acceptable to say “I” or “we” in scientific writing, but this convention has changed. Instead of writing: “The identity of the adhesin will be determined,” it is fine to write: “I will determine the identity of the adhesin.”

37. **Color.** It is fine to use color in your figures, if you think color aids communication of your ideas. It is also OK to use color anyplace else in the document if you think it will enhance communication. However, remember that your reader might be colorblind, so you cannot rely exclusively on color. Also, it is possible to have too

much of a good thing, i.e. excessive use of color might be distracting rather than helpful.

38. **Bibliographic software.** Be sure to use some sort of bibliographic software such as Endnote to manage your references. Trying to manage this task without software can take a horrifying amount of time (literally days). If you do not already have the software and know how to use it in conjunction with your word processing program, then obtain the software and practice with it immediately. You will not want to waste valuable time learning to use the software as the deadline approaches.

39. **Summary/checklist.** In addition to the grading criteria (point #12 above) and draft Specific Aims page criteria (point #29 above), the Microbiology & Immunology faculty considers the following features to be characteristic of a well-crafted research proposal. Ask yourself the same questions that they may ask about your proposal:

    - Are the Specific Aims themselves well crafted (e.g. designed to test a hypothesis or answer a question about how the world works, not simply perform a particular experiment)?
    - Are the Specific Aims independent of one another?
    - Does the Significance section make a good case for significance?
    - Does the proposal cover the key information needed to understand the planned project or is important material left out?
    - Does the proposal demonstrate awareness of the relevant literature?
    - Does the proposal critically evaluate the literature (e.g. point out potential gaps in knowledge, inconsistencies, questionable conclusions, etc.) or simply convey information?
    - Are the proposed experiments likely to actually work?
    - Are alternate experimental approaches proposed?
    - Does the proposal demonstrate awareness of the appropriate experimental methods or is a substantially better choice of method overlooked?
    - Does the author consider the possibility that his or her hypotheses might be wrong?
    - Are appropriate controls included in the experimental design?
    - Is there a plan to evaluate the statistical significance of the data?
    - Is the proposal logically organized? Do customized subheadings guide and inform the reader?
    - Is the proposal carefully prepared (i.e. modest number of typographical/grammatical errors, formatting inconsistencies, etc.)?

    GOOD LUCK AND HAVE FUN!