

of engineered integrin-specific fibronectin domains (as well as other potentially therapeutic proteins) into fibrin polymer systems. Additionally, utilizing various polyethylene glycol (PEG) configurations (e.g., monofunctional, bifunctional, and multifunction-branched) coupled with our engineered synthetic fibrin knob variants; we will demonstrate the ability to alter the polymer network ranging from complete inhibition of polymerization (in the case of mPEG) to the potential blend of fibrous and amorphous polymer (bPEG & mbPEG). Finally, the "designer" fibrin will be optimized for endothelial cell invasion and angiogenesis using specifically designed microfluidic chambers for *in vitro* angiogenesis assays and *in vivo* models of angiogenesis, i.e., the chick chorioallantoic membrane (CAM) model and subcutaneous wound chamber assays.

### Section 3: Approach

The Approach section is the heart of your Research Strategy. This is where you will provide the details of your research to convince reviewers that you understand what the work entails and have the resources and expertise to conduct the research.

According to NIH, you should use this section to detail the following:

- Your overall strategy, methodology and analyses you plan to use to accomplish your specific aims.<sup>9</sup> And if you have not included a separate resource-sharing plan, you should use this section to indicate how you will collect, analyze and interpret data, as well as any resource-sharing plans as appropriate.
- Potential challenges, alternative strategies and benchmarks for success that you anticipate to achieve your aims.
- If your project is in the early development stages, note any strategies to establish feasibility and how you plan to manage any high-risk aspects.
- Any hazardous procedures, situations or materials and precautions you will use to address them.

NIAID further recommends that you follow these strategies for this section:

- Describe the first set of experiments for each Specific Aim.
- Define the potential next steps for the aims, but do not describe them in detail.

This may lend itself to a flowchart or decision tree where you can indicate

that if you get result X, then you will follow plan X, but if you get result Y, you will follow plan Y.

- Provide enough experimental detail to demonstrate to reviewers that you understand what your proposal involves and can effectively conduct the research.
  - If you are a more experienced investigator, cite relevant work to show your expertise.
  - If you are a new investigator, indicate you can handle an experimental method, and particularly point out if you have used it before. If you have, cite it, and skip the description.
  - If you lack the expertise to accomplish the work, point out colleagues who do. Their Biosketches should highlight experience that supports their roles on your application. ✓
  - Outline your methods in less detail than you would in a publication. Provide more detail for unique or new methods, and keep graphics simple because they are clearer and can save space.
- Explain experiments to which you bring a unique ability.
  - If your first experiments are ordinary or contracted out, focus instead on those that you bring something unique to and that are interesting.
  - Next, describe your strategy, showing subsequent experiments based upon the results.
  - Draw connections between your personal statement and other Biosketch information, highlighting what you are doing that's different and what you do well.
- Incorporate milestones and timelines, assessing whether they are appropriate as you write. ✓
- If you do not need the information to support your case, leave it out of the Approach section. Reviewers will look for flaws and heavily penalize you for them. So do not give them ammunition by including anything you feel you do not need. ✓
- Include a timetable showing how and when you will accomplish your Specific Aims, noting any overlap of experiments and alternative paths.





NCI also suggests that your Approach include the following additional details:

- For early-stage projects, your strategy to establish feasibility and address high-risk aspect management
- New methodologies used and why you feel they are an improvement.

Further, NCI notes that you should number your Approach sections to correspond to your Specific Aims numbers. And you may include the preliminary data or progress report before the Specific Aims or integrate the data/report as part of your methods description for each aim.

The institute also recommends that you avoid excessive experimental detail by referring to publications that describe your methods. Keep in mind that any publications you cite should be your own if possible. And indicate why you will use one approach or method (if applicable) — and include the “how” and the “why” — rather than others because this will demonstrate that you simply did not overlook any alternatives. If you are using a complex technology for the first time, be sure to demonstrate your familiarity with the experimental details and potential challenges. If necessary, add a co-investigator or consultant who is familiar with the technology.

If your application involves proposed collaborations and offers of materials or reagents that have restricted availability, document this with letters from the individuals involved, NCI says.

### Allow Enough Time

✓ Because the Approach is so central to your Research Strategy section, you will spend most of your proposal-writing time on it. And it is what reviewers will spend most of their time evaluating. They will be especially careful to scrutinize it for potential problems, alternative strategies and benchmarks for success.

NIH's Office of Extramural Research last year looked at the five key criteria — Approach, Significance, Innovation, Investigators and Environment — and how well scores for each correlated statistically with an applicant's Overall Impact score. Based upon this analysis, the Approach score turned out to be the best predictor of the final impact score, with a correlation coefficient of 0.82.



### REMEMBER:

Reviewers will be especially careful to scrutinize the Approach for potential problems, alternative strategies and benchmarks for success.



The Approach section is also where many new Principal Investigators make one or more of the standard errors that are relatively easy to identify and describe. If this is the case, your Summary Statement may include such stock critiques as the following:

- The applicant is overly ambitious
- One or more aims are unfocused or underdeveloped
- An aim is just a fishing expedition for a missing gene or interactions
- ✓ • There is too little description of results analysis
- The applicant over-relies on a preferred hypothesis
- An aim is just too risky.

Reviewers may genuinely identify these flaws in a grant application, but they occasionally invoke them as a cover when they lack enthusiasm for a proposal and cannot precisely articulate why. Anticipating these critiques during your proposal writing is one of the best defenses you have, and knowing that the Approach score provides the strongest correlation to your Overall Impact score shows that this section is where you should devote most of grant preparation time.

Keep in mind that reviewers do not want to see details like which restriction enzymes you are going to use and which buffer goes with particular restriction enzymes or the brand of mass spectrometer you are going to use. What they are really interested in is your thought process regarding how you will accomplish each aim, including the following:

- Have you carefully thought through the problem you are trying to solve?
- What is your initial plan of attack?
- How likely is that plan of attack to work?
- What are the possible things that could go wrong? —
- What aspects of feasibility have you not yet demonstrated? —
- What is your plan for dealing with those problems if the experiments do not work?

To address the stock critiques above, some reviewers suggest that you spend a paragraph or two explaining the rationale of each aim, noting why you are doing it and outlining the experiment related to each one. You should also choose figures,

## TIP:

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tables or other visual data that allow reviewers to understand that you are the expert, careful and will do what you say you will.

You will also want to tie the different areas of your application together to better support your proposal. For instance, if you are demonstrating the feasibility of recruiting a target sample size in a psychosocial treatment outcome study, you will want to discuss your ability to recruit a specific number of participants in both the Environment/Resources section *and* in your Approach. The ability to recruit adequate patient population is that crucial to clinical studies. In this case, you would use one sentence in the Approach to document annual patient accruals and/or past successes in recruiting patients, and then use the Environment section to provide slightly more detail regarding why your institution is such a good place to do the clinical research with access to your target study population.

In addition, for research that involves nonstandard, nontrivial "data analysis" needs, be sure to sufficiently describe those needs in your Approach because this will inspire reviewer confidence in your project. With the Research Plan's 12-page limit, you should use approximately a half-page for this, or as much as a full page if your data analysis is particularly complex and integral to your success. If your project is a biomarker study or clinical trial, for example, remember that NIH will assign statisticians to specifically evaluate the statistical design and power issues, which you must discuss in your Approach.

You can also use your Approach section to provide details regarding novel aspects of your work. For instance, you plan to use a better, more innovative method of calculating sample size that reviewers likely will not recognize. Should you stick with the more conventional sample-size calculations? Or put the more sophisticated method in an appendix?

**Neither.** Instead, you should reference a publication that explains the new method and provide a brief description of its advantages in your Approach. If you feel you need a larger explicative discussion, seek your review officer's permission to submit it as supplemental material once you have your study section assignment.