NIH Specific Aims & Project Narrative

Grab Reviewers’ Attention and Get Your Grant Funded
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Overview

This report covers two key National Institutes of Health (NIH) grant application sections: Specific Aims and Narrative. While the majority of this information applies to R grants, like R01’s, R21’s, R03’s, it also applies to K awards and other NIH grants that use a Specific Aims page, including foundation grants. For example, both Howard Hughes Medical Institute and the American Heart Association utilize grants that require Specific Aims and follow the same grant outline as the NIH.

The goal of this report is to provide you with a strong sense of what the NIH looks for on a Specific Aims page and Narrative section of a grant application. Some of the data presented were developed with the NIH, and has also been a part of lectures at both Stanford Medical School, and more recently at Dartmouth Medical School.

The basic mantra for grantsmanship and writing a successful R grant is:

“there is no grantsmanship that will turn a bad idea into a good one… but there are many ways to disguise a good idea.”
Basically, no matter how strong your grant construction is, it will never transform an idea that is not relevant and significant into a fundable idea. However, if your application is poorly prepared, there are many ways to disguise a really good idea. A terrific research idea that is highly significant, has great impact, and aligns with the NIH mission must be written in a way that makes reviewers take notice. Remember, you’re competing with a lot of other excellent grants, so you must be able to stand out.

Gaining Reviewer Interest

The word “relevant” is important because that’s where dollars come in. The Congress reads the Project Narrative section that spells out the relevance of your research to public health. Because the NIH is funded by Congress, reviewers want to fund research in the areas that Congress is willing to put money into.

Jane Scott, who worked at the National Heart, Lung, and Blood Institute (NHLBI), said that:

“One reason for peer reviewers’ lack of enthusiasm on a grant is often that it does not address the primary scientific mission or interest of the funding agency.”
Here are five questions an NIH reviewer wants to answer “Yes” to when considering your grant application for approval:

1. Is your research important and significant to human health and disease?

2. Are you qualified?

3. Do you have the skills to complete what is spelled out in your proposal?

4. Will your research have an impact?

5. Is it relevant to public health?

Even if you regularly write R01, R03, R21 or other grants that are investigator-initiated proposals responding to a Parent Announcement (PA), you may not be adequately addressing a specific NIH Institute request for research, which are Funding Opportunity Announcements (FOAs) or Request for Applications (RFAs). These are issued to support research in a specific understudied area of science, or to take advantage of current scientific opportunities to address a high-priority scientific program.
What NIH Wants

Knowing what the NIH does and does not fund is critical to your grant’s success. There are numerous places on the NIH’s website (https://www.nih.gov) where you can find specifically what they are interested in. You should also look at specific Institutes if applicable (https://www.nih.gov/institutes-nih/list-nih-institutes-centers-offices), even if it’s not part of an FOA or RFA. Before you submit your grant application, it’s important to know that your proposed research will be of interest to the particular funding agency, even if a specific RFA or FOA is not followed.

What the NIH predominantly looks for are research projects that align with their mission and the research priorities of its Institutes, Centers, and Offices (ICOs). The projects that have a high significance and a large impact, as well as the ability to clearly move a field forward to address an unmet medical need, are the studies that NIH wants to fund.

When discussing the Aims page, it is important to understand what an NIH reviewer expects, as well as the words, “Significance and Impact.” These terms are tossed around by tons of investigators, but they’re rarely
able to verbalize what they think the Significance or the Impact of a grant is.

It’s also essential that you have a strong handle on what your Project Narrative is, and how it relates to your Aims and Research Strategy. Unless you nail down your grant’s Specific Aims and Narrative, you’re not going to get funded. It’s just that simple. You must know what you’re doing and why it’s important to the funding agency.

Scoring Criteria

The NIH assigns a score that is a synthesis of five scored criteria from one to nine. Overall, this measures the likelihood for a project to exert and sustain powerful influence in the research fields. These are the five R grant review criteria along with a quick definition:

1. **Significance** - What is the relevance to human health and disease?

2. **Innovation** - How original or novel is your Approach?

3. **Approach** - Will your Approach answer your Aims, are they feasible?
4. **Investigator** - What is your training and experience?

5. **Environment** – Are your facilities suitable, and do you have adequate support from your institution?

Of the five scoring criteria above, it’s essential that you include the first three in your Aims (Significance, Innovation, and Approach). In addition to the above items, your Narrative should also contain the Significance, and although your Environment and Investigator criteria are not normally included in the Aims, they can be. I’ve seen Aims pages that include something very unique about the research team. This can be an extremely strong statement that shows real synergy between various investigators. It indicates that your team will be able to look at a particular problem in an interdisciplinary or multidisciplinary way. Basically, you can say something about yourself, your team or the environment you’re doing it in, but you have only one page.

**What NIH Doesn’t Want**

It’s also important that you clearly understand what the NIH is NOT really interested in. If your research
doesn’t have any clear Significance or Impact towards diagnosing, understanding or treating a disease, you won’t get the time of day from the NIH. In addition, basic research ideas with no clear Impact on clinical translation, or those that have been extensively pursued and are well-worn, are also not of interest to the NIH. Research that’s been done over and over, and is perceived as incremental and adds little to what’s known has little chance of getting NIH’s research money. You see this a lot when previously funded R01s are up for reapplication or renewal. These days, renewals aren’t as easy to get. It’s actually better to go for a new grant with a new idea that would be based on your original research than to try and get your funding renewed.

Grant Application Rejection

Highlighting the reasons your grant may be rejected is important as well. As you review your grant, be sure to keep these items close to ensure you don’t make these critical mistakes again:

1. No Significance: Your research doesn’t fill a critical knowledge gap or an unmet medical need – meaning it isn’t relevant or significant.
Basically, if there’s no clear public health relevance or significance to your grant, you’re probably not going to get funded. This report examines what Relevance and Significance really means to the success of your grant.

2. No Impact: Your grant contains no clear impact on your field. It’s essential that you understand what the word “impact” really mean to the NIH.

3. No Relevance: Your idea isn’t relevant to the mission of the NIH or an Institute, and relevance to the NIH mission is very important.
The Aims Page

Your Aims page must clearly describe to the reviewer what problem or gap in knowledge your research is tackling, and how it will impact research going forward. Also, it must ONLY be one page, be formatted with text 11-point type or larger with at least half inch margins. Getting this right is essential to your funding.

Many esteemed scientists and successful grant writers will tell you that most reviewers will only read your Aims and Abstracts to make up their minds about your project. Few reviewers actually dive into the detail of your proposal to support their opinion. Basically, your Aims and Abstracts are window dressing for the rest of your proposal. If readers don’t like what they see, they aren’t going to read anymore.

In fact, all successful grant writers know the secret to writing a great grant. It’s the first page of your application. Most reviewers assign about an 85% to 90% accuracy score just by reading this first page. In other words, just by reading this page, a reviewer can say,

- “This’s fundable.”
- “This’s not fundable.”
WRITING A WINNING SPECIFIC AIMS AND PROJECT NARRATIVE

• “This’s going to have a high score.”

• “It’s probably not going to have a high score.”

• “It’s a highly significant problem that we have been wanted to tackle for a long time.”

• “I’m excited about what they’re doing.”

• “I’m not excited, and this is not a major problem that needs to be addressed.”

By reading this one page, reviewers will decide if your proposal is going to the top of the pile to get re-reviewed, or the bottom of the pile to get rejected.

Your Specific Aims are the most important part of your grant. However, Aims are also the most difficult. They are difficult to write because they contain literally everything about your grant on one page. It’s important to write your Aims so they don’t skip any important details, while also not getting bogged down with information unimportant to the reviewer.
Writing Your Aims Page

Many grant writers get three-quarters of the way down their Aims page and say,

“Oh my God, I’ve only got maybe half a paragraph left to describe my experiments and what my expected results will be.”

This indicates how difficult it can be to write your Aims page in a balanced way. You must convey enthusiasm for your project. The flow of logic on this page must be compelling, and in combination with your Narrative, your Aims page will be used by the Scientific Review Officers (SRO) to recruit reviewers to securitize your grant application for funding.

You should write your Specific Aims page first. Then, as you work through your grant, revise your Aims page to ensure it coincides with your application. Your Aims page must contain five important points about your proposal:

1. Why do you want to perform this research?
2. Why is the research significant?
3. What important problem are you tackling?
4. What are you going to do with the research results?

5. How are you going to do it and what impact is it going to have?

Trying to write your grant proposal without clear knowledge and understanding of how these things will fit together is a waste of time. If you get mired down into the research strategy, without outlining it or without having a master plan, you will likely spend valuable time and energy on an unbalanced proposal with no direction or flow of logic, and ultimately get rejected.

When you start writing your Aims, you must ask yourself these important questions:

- Will reviewers see my research as tackling an important problem in a significant field?
- Will reviewers view my Aims as capable of making new discoveries in my field?
- Do I expect to find something new that will help science move forward?
- Will reviewers regard my work as new and unique?
- Is there something novel and different about what I’m doing?
• Will reviewers view my Aims as capable of exerting a significant influence on the research field (Impact)?

• Are my Aims clear and easy to understand?

Have colleagues in your field read your Aims page and provide you with feedback regarding their clarity and understandability. For example, if you’re studying a specific area of neuro-oncology, you should hand your Aims over to somebody in an allied field. It’s important that you ask them to provide you with answers to the following questions:

• Do you think the Aims are clear?

• Are my Aims easy to understand?

• Are my Aims logical?

It’s crucial that your Aims are clear, easy to understand, and logical so reviewers can fully comprehend your research goals as they read through the rest of your proposal. It is recommended by the NIH that you,

“State concisely the goals of the proposed research and summarize the expected outcomes, including the impact that the results of the proposed research will exert on the research fields involved.”
If your Aims page doesn’t encompass this it will be hazardous to your grant. You MUST provide it to get approved. The NIH also instructs you to state the specific objectives of your research in your Aims. You should include:

- Test a stated hypothesis,
- Create a novel design,
- Solve a specific problem,
- Challenge an existing paradigm or clinical practice,
- Address a critical barrier to progress the field of science or,
- Develop new technology.

You may be doing all these things, but it’s important within those criteria to address what you’re doing to overcome a specific gap in knowledge.

The Four Paragraph Template

The four-paragraph template is used by many grant writers, as well as the NIH, and is what many reviewers expect to find in a grant. It follows a logic where the first paragraph identifies the problem or need, as well
as the knowledge gap that we're addressing. Your solution to fill that gap in knowledge is represented by the Aims, and how your discoveries will impact medical research. In your Aims, you want to address the overall grant goals.

**Paragraph #1: The goal of your specific R01.**

For the first paragraph, you must define the critical need and gap in knowledge you are trying to fill, also known as the problem you are trying to solve. This is a short background with current knowledge leading to the important problem that you will solve. It may be helpful to use the words “gap” and “knowledge” in your Aims to ensure that you’re clearly identifying the gap.

**Paragraph #2: Your long-term goals.**

The objective of the second paragraph is to solve the problem that you just stated in the first paragraph. You fill the gap by proposing a central hypothesis and rationale that fits into your long-term research goal, which is to solve this stated problem.
Paragraph #3: The continuum of your research.

The third paragraph contains your Aims: the objectives that test your hypothesis directly related to the need that you have identified.

Paragraph #4: How this grant will help.

Your fourth paragraph is the payoff to the NIH: the expected outcomes leading to Impact. Are you addressing a particular NIH need? If the grant is unsolicited, it would be good for you to mention that.

You must convey that the probability that your study will be successful and exert a powerful and sustained influence on the field. This is your Impact. If your research won’t work, it has no Impact, even if it has a strong Significance.

Your First Paragraph

Your first paragraph is critical. You’re going to have to convince your reviewers that there is an important gap in knowledge that needs to be addressed. Then, you must show that your research will solve this unmet medical need.
Your opening sentence must grab the reader’s interest, and immediately establish the relevance of your proposal to human health. You may be doing work in rats, monkeys or cells, but your research must ultimately have relevance to human health and disease. You must persuade reviewers that by supporting your proposal, they’ll be helping the NIH accomplish its goals. Therefore, it’s important to identify what specific areas of research the NIH is interested in tackling.

The first paragraph looks like this:

- What is known?
- What is unknown?
- What is needed?

Start with a statement regarding what’s known about the specific problem you are addressing in your application. By starting with the current knowledge, you’ll help the less informed members of your review panel get up to speed in the subject matter. Then, identify the gap in knowledge that’s holding back the field and what you will address with this application. The first sentence in your Aims should never look like this:
1. “Cigarette smoking is a recognized causal factor of lung cancer that costs the healthcare system $3 billion a year,” or

2. “Lung cancer is the leading cause of death among men and women in the USA and responsible for so many deaths.”

This angers reviewers because it’s not the problem you’re studying, rather you’re just regurgitating Centers for Disease Control and Prevention (CDC) statistics to the reviewer. You need to identify the gap in the knowledge that will help. Using the example above, a more effective way to write your first sentence might be:

1. “Although overall rates of cigarette smoking in the US have decreased in the last 20 years, smoking rates have actually increased among low-income women of child-bearing age in the last 10 years.”

2. “Failure to identify regional lymph node metastasis in the 40,000 US patients a year with surgically resected lung cancer is associated with a three-fold increase in recurrence and decreased overall patient survival.”

As you can see, the second examples expand past just the higher-level issues and represent specific gaps in knowledge that need to be investigated.
Your identified gap in knowledge must make a case for a real problem, and argue that there is a critical need for your research. It’s extremely important that you understand that the NIH wants to see that critical unmet need in the first paragraph. Also, you can increase your chances of funding if you tie your identified problem to a specific NIH area, such as the National Institute of General Medical Sciences (NIGMS). Hopefully, this will lead your application to be reviewed by this Institute, giving you the best chance for approval possible.

Here’s an acceptable example of a first paragraph showing known, unknown and need:

“Reestablishing the skin’s protective barrier through wound healing is significantly compromised in certain common chronic diseases such as type II diabetes. Open wounds lead to serious infections if not treated. Steroids and antimicrobial hydrogels are currently the standard of care in open wounds after surgical debridement\(^1\text{-}^3\). However, these treatments result in adequate wound closure in only 32% of serious wounds, leading to systemic complications and death in 80 patients a year, which is not yet fully understood. The reason..."
for poor wound healing involves wound microenvironmental changes in pH, calcium, magnesium, and alterations in microvascular, which haven’t been adequately studied in wound healing. This critical gap in our understanding of wound healing has been recently identified as one of the central goals of the NIDDK, and the subject of an RFA. Addressing these unmet needs will better help us better to understand how wounds heal in order for researchers to identify therapeutic targets and strategies."

Please note that these can be cited with references to show that you’re providing background (the known). This may not be the most elegantly written first paragraph, but it shows the progression of the argument that goes from known, to unknown, and to the gap.

**Your Second Paragraph**

Having established a gap in your first paragraph, your second paragraph is where you provide your solution to the problem. Basically, a fix for the critical need.

Your solution must be hypothesis-based. What is your overall objective with this application? It might be
to develop a map of a wound microenvironment leading to identification or development of biomarkers for wound healing. This may be the objective or your application, but your research is a continuum. You may be looking at developing biomarkers of wound healing and identifying treatments that target them (the biomarkers).

Your second paragraph should contain the immediate objective of your research, and how it fits in your long-term goal. In this paragraph, you go from the broad to the narrow. It begins with the long-term goal, the continuum of your research over multiple periods of grant support, your big picture, then your overall objective for this application to fill the knowledge gap that you just mentioned. Every grant should be a hypothesis-based application. Why are you doing this work? What new things will become possible that aren’t possible now? New therapeutics, new tests, new paradigms, that’s your rationale for the second paragraph.

Your Third Paragraph

Next, your third paragraph is your Aims. This is a step-by-step development of the key objectives that will address the problem that you stated, based on your identified objectives.
Here are several points to consider when writing your third paragraph:

1. **Hypothesis-based**: Whether you’re testing a central or specific hypothesis that addresses the problem and fills the gap, your Aims must be very specific, measurable, and doable in the time frame of your grant.

2. **Aim Dependence**: The other problem found in a lot of grants is that one Aim is dependent on another. In other words, if you don’t reach the goal in your first Aim, the second and third Aim will fail. It’s important that your Aims are related by the hypothesis and the overall objective of your grant, but independent of one another.

3. **Detail**: A big problem found when writing Specific Aims is way too much detail in the experimental approach. You should keep it short, only a couple of sentences. Each Aim should show a part of how you answer your original hypothesis.

4. **Aim Count**: The next step is figuring out the number of Aims to include in your proposal. It’s difficult to specify exactly how many Aims for each type of mechanism, but you must ask your-
self realistically: “What can I realistically accomplish? In the two years of an R03 or an R21 or in the four or five years of an R01, what is really possible to achieve?”

5. Goal Reality: Over-ambitiousness is a very common problem. Consider only three or four Aims for an R01, and typically one or two Aims in a smaller R03 or R21 is acceptable.

6. Specificity: Another problem found when writing the Specific Aims is the use of non-specific and vague statements. Examples of insufficient specificity: “To study the effects of ... To explore the reasons for ... To better understand the effects of ... To investigate causes of ... To compare the ... To describe the ...” These examples are very unclear as to what you’re going to do; the Aim must be very specific. For example: “We're going to measure levels of calcium and magnesium and pH in the wound microenvironment over 21 days in an established rodent wound healing model.”

The next sentence or two should then give the reviewer a taste of how you’re going to accomplish this (without a lot of detail). Aims are very difficult to write because you must condense them down.
It’s very important to keep this to one or two sentences. For a two-sentence example:

“Male Wistar EK-21 rats with incisional dorsum skin wounds will be blindly scored for evidence of hemorrhage, ulceration, fibroblast contraction, and scab formation using standardized assay. Wound extracellular Ca\(^{++}\) and Mg\(^{++}\) and pH will be measured daily and correlated to the patterns of wound changes over 21 days.”

Here, the model is given, but there is no mention of what the assays are. The other way you could state this Aim is, “To test the hypothesis that,” or you may say, “We want to correlate.” Instead of measuring these you might correlate the changes in wound patterns, or wound changes over 21 days to levels of calcium, magnesium, and pH. Whichever way you state it, it must be doable, testable, and very specific.

**Your Fourth Paragraph**

This is where you bring in a sentence or two about how novel or innovative your work is. Your research doesn’t have to create a new paradigm or use a totally new method, but it can shift a current method or
paradigm. You may be using established assays, but applying them in a unique way that’s never been done before. You may be looking at a series of three or four assays to test antimicrobial compounds in various labs using tried methods, but in a unique way, in which the compounds flow in a pattern that’s never been looked at before.

You need to think about what is unique about the way you’re approaching the problem you’ve identified. Specifically, what is the Impact of your study? This last paragraph, essentially, is really the NIH’s payoff. Why should they even fund this work? How is it going to influence the field going forward? Perhaps you’re developing a new treatment, a new vaccine, a disease model or diagnostic tool. It’s something that you’re going to give the NIH that is going to push the field forward in a way that has eluded science up to this point.

It’s important that expected outcomes are very specific and credible. It’s the return on investment for the NIH. You should never write them in the future tense because you should know pretty much when you write your proposal what you think will happen. For example, “We expect to determine this,” or, “We will expect to find these things out that we didn’t know before.”
Here is an example of how to begin your fourth paragraph:

“By the end of our study we expect to fully characterize the wound microenvironmental changes in pH, calcium and magnesium, and changes in microvasculature, providing in-depth insights into wounds as they heal. This will be the first study using an established wound model to correlate wound healing parameters to specific microenvironmental changes in pH, calcium and magnesium, and alterations in microvascular using novel high throughput assays.”

After you’ve identified for reviewers that what you’re proposing hasn’t been done before, follow with a statement like the following:

“Insights into the mechanisms of wound healing will provide knowledge to scientists and clinicians, to help identify specific therapeutic targets and strategies to more effectively manage wounds as they heal.”

Outcomes MUST be specific and credible. You don’t know what you’re going to find, but you must have a strong belief that your discovery will have an Impact.
This is the purpose of doing the research, so it’s extremely important that this paragraph is well crafted.

**The Use of Specific Language**

In the Aims page, as well as Significance and Approach, you want to use specific language that will identify areas of research that the NIH is interested in that your work addresses. To say things like, “Our proposal addresses three objectives of the NCI RFA,” is a good way to state your interest in the Request for Application (RFA). Of course, if you’re not applying for that because it may not be directly spot on for your research, it still has information in it. It doesn’t directly apply to your proposal, but there might be a couple of objectives that you will address in your research.

Here is another example of how to use specific language:

“Our Specific Aims address two objectives of the National Institute of General Medical Sciences, namely…”
Another option, with more detail, would look like this:

“Our research is in direct response to the NIH 2016-2020 strategic initiative for Brain Research Through Advancing Innovative Neuro-technologies that addresses next-gen invasive devices to record and modulate the central nervous system of patients with spinal damage.”

This is a new interesting area of research, with an unmet need and knowledge gap. If your work addresses these various types of things, you should state it as clearly as possible. You want to be sure that reviewers understand that this is a critical and needed information.

You must spell out that the problem you’ve identified leads to a gap in knowledge and is a critical need. The hypothesis-based solution that you’re putting forth and the objectives that you’re going to tackle in this grant will lead to some expected outcome with an Impact and longer-term goal for your future work. This all goes back to the original knowledge gap.
Let’s look at one specific proposal that was put forth. Here’s the problem:

“Colon cancer is a fatal disease if not detected early. Current medical practice in the US is screening colonoscopies for everybody over the age of 50 years old, but colonoscopies are expensive and invasive. Screening for occult blood in stools is inexpensive, but it’s ineffective, and many cancers are missed. A blood test that could accurately detect colon cancers would save lives. Current approaches for measuring proteins in blood are relatively insensitive and unlikely to detect cancers early enough. Human variability and low signal in these proteins mean many independent patient samples must be measured.”

In the paragraph above, the gap in knowledge is represented by the words “Current approaches.”

Next, you should continue by highlighting your proposed solution:

“New proteomic technologies developed by my group offer both the sensitivity and throughput needed to identify and validate biomarkers or detection of colon cancer early. Our long-term goal is using bioinformatic
methodologies. We will develop key biomarkers for other cancer types, such as lung, pancreatic and brain, for high throughput proteomics. We hypothesize that colon cancers can be more effectively detected using sensitive blood biomarkers.”

Then, on to your action plan. It should be short and to the point:

“To identify plasma proteins associated with the early stages of colon cancer. These measurements will be applied to a unique cohort of colon cancer patients available from clinical collaborators.”

Finally, you should finish up your second Aim with a quick summary sentence. If you’ll be using software tools, mention them. You can also use acronyms if you wish. However, keep in mind that the text should not be long.

“To carry out a novel bioinformatic analysis of over-represented proteins for enrichment of specific functions.”
Carrying forward our example, our third Aim is:

“To select and validate the candidates that you find. They’ll be selected on the basis of functions known to be associated with carcinogenesis and will be verified by orthogonal approaches. The top 10 candidates will be assessed in 1,000 prospectively collected blood samples from early stage colon cancer patients using a novel high throughput proteomic approach.”

The last paragraph should look like this:

“The end product of this research will be an accurate blood test for early detection of colon cancer without colonoscopy. Our approach will use many previously successful methods, seen in our preliminary results, to increase the probability of success to reach this goal. Successful demonstration of this approach in colon cancer will enable application to other cancers in need of early detection. Future directions of this research will include the application of a systems biology approach to the large data sets generated in the discovery phase that will provide new insights about the earliest stages of colon cancer.”
The National Cancer Institute (NCI) says, “The prostate, lung, colorectal and ovarian trial will determine whether screening tests will reduce the number of deaths from these cancers.”

That is actual wording from a proposal, so that is the kind of information that they want to see in the last paragraph.

**Specific Aims Gone Wrong**

A major issue with Specific Aims is the lack of original or innovative ideas. You must be specific and focused. It might be helpful to ask yourself the following questions to help target your Aims:

- Are there any risks with the work?
- Why is it important to pursue?
- How could knowledge move the field forward if the Aim wasn’t even met?

Also, you must justify your Aims. You’ve got to show a relationship to what’s known and what’s unknown. Finally, you must have a hypothesis-driven proposal.
Here are actual reviewer’s comments critiquing a poorly written proposal:

“Proposal looks more like a collection of experiments in which the applicants are simply listing experiments according to their expertise in specific techniques, instead of testing an underlying hypothesis. Our enthusiasm was dampened by a lack of hypothesis-driven by a specific mechanism.”

Your Aims must be thematically related to form a cohesive unit. You want to think of a central hypothesis that unifies your Aims. Also, you should avoid inter-dependent Aims unless there’s no doubt that the early goals will be achieved. A look-and-see stance is not a good way to write an Aim, and reviewers don’t want to see it.

Also, don’t describe techniques, as this gives the reviewers the impression that you aren’t focused, and you haven’t really thought the proposal through. As previously mentioned, one to two Aims for R03 or an R21, maybe two to four with an R01 grant. Be sure to address Significance and Impact, because If you don’t the reviewers will not be interested when they read your proposal.
One study in *Annals of Internal Medicine* back in 2005 showed evidence of problems in 66 grants. Some of the main issues included:

- Gaps in knowledge weren’t clearly articulated
- Overstated, overly ambitious and unrealistic goals
- Grants were poorly focused and inadequately conceptualized
- Hypotheses weren’t clearly articulated
- No clear statement on expected results and impact.
Project Narrative

The Project Narrative is a project summary, which is really a succinct description of your work. It is not your Aims, rather it’s a concise description, in lay terms, of how your work will affect public health.

Unfortunately, many people gloss over the Narrative. This is a mistake as this part defines the relevance of your proposal. The NIH asks you, in no more than two to three sentences, to describe the relevance of this research to public health in plain language. It is important to note that Congress reads these. Therefore, it should be understandable by the general public, a non-scientific audience. It’s also very important to have this nailed down. People will want to read your Narrative in the NIH RePORTER, where it also can be found.

Your Project Narrative should always be written after your Aims page. It’s often the first thing read by reviewers and Congress. Potential funders will read this to determine if the project fits within an agency’s mission and support, as well as the project’s potential
to improve public health. So, your Narrative must be clearly articulated, and be written to get the attention of the reviewers. Also, remember that non-scientists will be reading your Narrative, so be cautious not to write it too technically.

What’s the best way to write in lay language and still get your scientific point across? You should consider four things:

1. What disease state or problem am I tackling?
2. What do I plan to do to overcome the problem?
3. How will it help diagnose and treat people with the disease?
4. How is this relevant to human health?

Below are a couple of examples:

Example #1:

a. Unfunded: You’ll note that the language below is uninteresting for anybody who is not technically adept in this field. It’s too technical the way it is written. It doesn’t provide a very clear statement of importance or how it relates to human health.
“Legionellae pneumophila uses a specialized type IV secretion apparatus, known as the Dot/lcm system, to secrete over 150 effective proteins directly into the host cell. The translocated bacterial effectors establish a vascular niche that supports the ….”

b. Here is an example of how it should be written:

“Legionnaires’ disease is a rapidly progressive, deadly disease, caused by the bacteria legionellapneumophila, which replicates in cells of infected individuals (host cell). To replicate inside the host cell, bacteria injects 150 proteins. Our research will use a large-scale approach to identify the targets of these injected bacterial proteins, thereby identifying the host cell proteins that are destabilized by the injected bacterial proteins.”

“Once we identify which bacterial proteins are manipulating which host proteins, we can disrupt these interactions, halting the disease. This will lead to new, highly effective classes of antibiotics to treat bacterial infection responsible for this disease.”
The following examples illustrate ways to reword the project narrative to better communicate the value and intent of your application to a general audience:

a. Example 1: BEFORE

PUBLIC HEALTH RELEVANCE: Heart failure (HF) is a debilitating disease with poor prognosis. The proposed research aims to investigate the molecular and cellular mechanisms that contribute to the development and progression of HF. Successful completion of experiments outlined in this proposal will enhance our current understanding of an established HF signaling pathway and may provide a novel therapeutic strategy for the treatment of HF and associated sympathoexcitatory diseases.

b. Example 1: AFTER

PUBLIC HEALTH RELEVANCE: Heart disease is a leading cause of death in the U.S. Medications currently being used to treat heart disease are helpful to many individuals but do not work on all patients. Therefore, there is a vital need to develop additional drug treatments that will provide multiple approaches for treating all individuals afflicted with this
debilitating illness. This research should provide important information that can be used in developing new heart disease therapies.

a. Example 2: BEFORE

In this study, researchers at three sites across the U.S. will work together to develop and validate an integrated prevention program, SafeSex4.0, to reduce the risk of HIV infection in men who have sex with men (MSM) in suburban communities. This prevention program will offer comprehensive, integrated healthcare services, and will enhance the health of MSM by reducing risky behavior, providing greater access to care and services, and establishing networks of social support. The findings obtained from this study may be used to inform decisions about healthcare policy and implementation of clinically-effective interventions.

b. Example 2: AFTER

Anti-retroviral drug therapies and behavioral intervention programs have been effective for treating and reducing HIV infection. Yet although overall infection rates have declined, HIV infection rates for some populations in the
US continue to rise. Therefore, it is important to develop additional clinically-proven prevention programs, such as the one studied in this project, to fully reduce the incidence and prevalence of HIV infection across the US.

It is crucial that you understand what a successful grant looks like. Make sure you go to the NIH RePORT-ER and look at grants in your field. You should read their Project Narrative statements to get a better sense of what has been said and what has been funded. Looking at sample grants can be very helpful. The National Institute of Allergy and Infectious Diseases (NIAID) has an outstanding website that gives you R01, R21, R33, and different K01 awards. The entire application is in there, along with the summary statements. You can find this information online at https://www.niaid.nih.gov/grants-contracts/sample-applications.

The other thing to consider is looking at various research priorities for all the different Institutes, the ones that you’re most interested. Pay attention to key objectives, key initiatives, and areas that they are interested in funding.
Searching for Funding Opportunities

Some of the research objectives found on agency websites have a funding opportunity attached to it. However, it’s also important to look at the actual Request for Applications (RFAs) of those Institutes to see what they are looking for. Without this knowledge, before you start work, you won’t know to include it so your chances of funding will be significantly less.

For example, if you look at the National Institute of General Medical Sciences (NIGMS), they fund a significant amount of R01’s every year. Accordingly, there are a lot of programs that you may be missing if you aren’t aware of which Institutes fund what, this requires a fair amount of research. Possibly, you have colleagues in your lab that could go and start looking up some of this information using the NIH Guide to Grants and Funding found here: https://grants.nih.gov/funding/searchguide. The goal is to uncover some RFAs that address your work or some initiatives that you may find of interest. It’s very important that you know what organizations are interested in funding your area of research.

As previously mentioned, the NIH RePORTER (https://projectreporter.nih.gov/reporter.cfm) allows
you to do queries; you can search through keywords, PI names, institutions, as well as look at study sections and what they’re funding. That’s very important to know, as it gives you a leg up on the competition.

Here are a couple of pieces of advice that peer reviewers put forth from the NIH website That succinctly summarizes the essence of this report.

Martin Philbert from the University of Michigan says: “If you don’t immediately convey the essence of why this work is important, then no matter how good the idea is it’s lost. You want to convey clearly and repetitively what you want to do, why it’s important and how it will advance the science.”

Another quote listed from a reviewer: “The most common error, particularly with new investigators, is over ambitiousness, trying to cover too much territory with the time allowed, and that’s reflected in the Aims page.”

David Grainger: “You can read many proposals, and one stands out as a wonderful piece of writing. For me these contain a lucid style, a compelling scientific, creative, idea, and this idea of impact, moving science forward towards a clinical end that is credible with a boost in capacity to a patient popula-
tion with an unmet need.”

**One Last Thing**

One of the most important things to remember is that you MUST address the critical need that the NIH wants to fund. Your grant must have a high impact and great innovation.

Also, it’s not enough to include the information outlined in this report in your NIH grant application. It must also be beautifully written. No matter how good your idea is, you won’t get funded if the English isn’t clear, the writing is sloppy, unclear, not concise or illogical.
Frequently Asked Questions

Question: Why are Specific Aims important?

Answer: There are many reasons why Specific Aims are important. It’s the first thing that a reviewer is going to look at, no question. They may read the Abstract and the Narrative, but they are definitely going to read your Aims page to start with.

They’re not going to be thumbing through your Research Strategy. They want to see what your work is about. You must convey clearly in that page what you want to do, why it’s important to do, what gap in medicine you’re addressing and how it’s part of your research. State clearly your three or four Aims that get at the hypothesis that you’ve put forward, what you expect to find and how it’s going to help research going forward.
If that isn’t clearly nailed down, the rest of your proposal pretty much will be window dressing. I think that if your Aims page doesn’t really nail it for a reviewer, it’s not going to get a good score. It’s pretty rare for a reviewer to read a poorly written, unclear Aims page, and then read the rest of the proposal and say, “Now this is much clearer.” It’s unlikely that would happen. This is the page where it’s going to make or break your proposal. It’s probably the most important part of your research grant.

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**Question:** What about technology development projects?

**Answer:** If you’re developing purely a new technology, it wouldn’t normally be the basis for an NIH grant. It’s more likely that you’re doing innovative business development with an industry partner or something through a Small Business Innovation Research (SBIR) grant or something like that.

NIH R01 and R21 grants are usually hypothesis based. Usually, you can find the
hypothesis that your research is revolving around. Meaning, you’re asking questions that haven’t been answered, and it has a hypothesis.

Question: Why should the Aims stand alone?

Answer: If your second Aim is dependent upon finding the answer to the first, it’s going to kill your grant. Reviewers will assume that you won’t be able to go any further if you can’t prove your first Aim.

It’s very important that one Aim doesn’t depend on another one. They must be interrelated and be held together by your hypothesis, but they should be able to stand alone and be solvable without one of them failing. It’s also important to state that if one Aim fails, it will still provide you with knowledge related to your goal. It’s critical not to build a series of three or four Aims all of which depend upon one another, because it can be death for your grant.
Question: I’m planning to submit an R21 and I am having trouble understanding how an exploratory research grant should look different than an R01 grant. Are there different expectations regarding the Aims, and how clearly they should feed into my broader research plan? Please explain.

Answer: There are significant differences between the R21 and R01, beginning with the number of pages that are allowable for your research plan. For an R01 it’s 12, in an R21 it’s only six. The R21 is also designed to fund exploratory research within a short period of time, and a smaller budget, to assist in developing pilot data or a feasibility study. You can only request a maximum of $250,000 for a non-renewable two-year project. Due to these factors, the R21 will only have one or two Aims, three max.

With an R21, you’re exploring a new area, and there’s probably not a ton of preliminary data available. Unlike the R01, preliminary data is not required to apply for an R21. However, it is strongly recommended you include some. You are asking the NIH to
fund a high-risk project that may not yield any reproducible results. With preliminary data, you lessen this risk and can create a more favorable score.

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**Question:** Is it a good idea to have a timetable? How should I set it up?

**Answer:** Aim should have objectives that you must meet before you answer the question. You can think through each Aim to determine what specific objectives you must reach before you answer the Aim. Those could be put in a table, and you can say this will take place in year one, year two, or year three. Just the objectives for each Aim and you may have several.

If you feel it’s important for the reviewer to get a sense that you thought through these four years and what you might be able to accomplish. This type of a table, or timetable, could be put at the end of the Research Strategy section.
Question: Should I put expected results after Specific Aims?

Answer: The four-paragraph template outlined in this report is a general template. Every grant’s going to be slightly different. Whatever makes the most sense for your grant or your proposal, you should put in.

The expected results should be at the end in the last paragraph saying, “By the end of our study we expect that we will have developed this new technology, we will have found these things.”

If you want to put it into each Aim, keep in mind that it’s going to lengthen your Aims page. But if it’s just a short sentence, it would not hurt. The main thing is that you address your expected results, and you give the reviewer that information.

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Question: Can you clarify what you meant by “Aims should not be dependent?” For example, if I propose a study examining the effect of a certain treatment, the first Aim might be
to identify responders and non-responders of the treatment. The second Aim might then be to identify determinants of the responders. Are they dependent on each other?

Answer: If you’re pretty sure you’re going to find that 10% of your population is responsive to this treatment, that’s perfectly fine to write your Aims this way. However, I wouldn’t put an Aim that is that simplified. If that’s the general idea of the Aim, that’s fine, but it should be very specific about what you’re doing, and how you’re determining it.

Question: How important is it to mention aspects of the Research Strategy in the Specific Aims?

Answer: Your Aim should be followed by how you’re going to accomplish it. You’re measuring something, you’re comparing something, you’re doing something very specific, and you don’t want to give a lot of details. In this case, you can insert references to indicate specific assays or methods that have been used by your group before, but this is not the place to do a lot of that.
Your preliminary, or early results should be written as part of your Research Strategy and be included with a lot of detail. Your job is to take that Aim and write a one to two sentence summary of what you’re going to do. It’s very hard to write because it’s a lot of information that you must convey in a short space. Therefore, I wouldn’t get into the habit of putting references or providing too much detail.

Question: In my opinion, using technologies like proteomics to identify correlations in unknown molecules to a specific disease condition falls into the category of a fishing expedition. Can you comment on how to avoid such criticism?

Answer: You’re using proteomic methods to solve a specific disease, or you’re doing it as part of a methodology to answer an unmet need. Therefore, it should not be considered part of a fishing expedition or a waste of time.

You should go to your research team and ask the question, “What do you think the
best way of tackling this is?” However, you should be starting it, “What is the specific problem we’re studying here, and how is the best way to get at it?”

There is always the possibility that people on the review committee may disagree with the way you’re approaching your research. A good way to narrow your risk is to look up areas of research that are similar to yours on NIH RePORTER. Read some of the things that are being done.

Question: How is the Project Narrative related to the application and why is it so important?

Answer: This is something that the Congress reads. These statements are compiled and read by certain congressional committees that are in the healthcare field, working with health and human services. It’s not the same thing as the Significance, but it is relevant.

If you’re putting forth a good grant that is addressing an important problem that has eluded science to this point, you must
explain the relevance to human health. Maybe this work is being done in healer cells; maybe it’s being done in Wistar rats. Ultimately, you’re doing it for human health, and your proposal requires some relevance to treating or diagnosing diseases that the NIH is interested in. It’s extremely important that you have identified this medical need. It’s hard for most investigators to write this, however because they find it very difficult to write in lay language, so simplification is key.

Since your Project Narrative is two to three sentences, and writing in lay language can require the use of a lot more words, you should visit the NIAID website and look at their examples. You can also go to NIH RePORTER and look at the relevance statements to get a sense of how they are written. It’s extremely important because a lot of times a reviewer will look at those right away and think, “I just want to read a short blurb of why this is important to human health.”
A perfect Project Narrative relates directly to your Aims page, and that is where you explain what that relevance is.

Question: I’m not sure what we will discover in this research, so how can I write my expected outcomes?

Answer: Anybody doing research pretty much knows outcomes are based on previous preliminary data or previous research. If you’re writing an R01 for example, you’ve already done a fair amount of work in this field. You’ve amassed a certain amount of data; maybe it’s part of the grant, maybe it isn’t. You should kind of know just by being an expert and knowing the kinds of findings, seeing the data and results that have come forth previously. Yes, you will not be able to say exactly what is going to happen, but you can provide the best guess based on what you’ve done in the past.

It’s kind of a conundrum because you’re asked to provide the NIH with expected
findings, or what do you expect to find, when you haven’t even done the work. But most researchers will agree that they have an idea of what they think they’re going to find. They may be wrong, but if you’re writing a full R01 grant that’s based on previous research in the field, they’ll have a good idea of what’s going to come forth from the work.
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