Writing Effective Specific Aims

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A successful proposal is an effective act of communication

The key to good communication is knowing your audience and putting yourself in their place

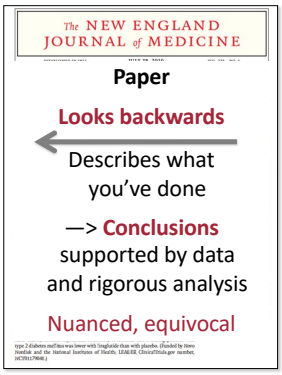
"The Reviewer at Work"

The audience for your research proposal . . .

Your goal is to excite and persuade your reviewers

How do you want the reviewers to react to your proposal?

First, writing a grant is different from writing a paper



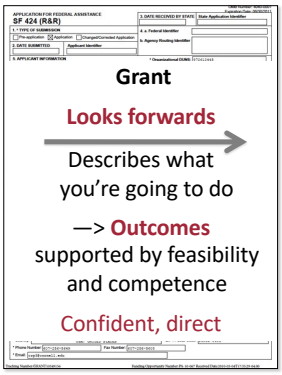
Paper

Looks backwards

Describes what you've done

—> **Conclusions** supported by data and rigorous analysis

Nuanced, equivocal



Grant

Looks forwards

Describes what you're going to do

—> **Outcomes** supported by feasibility and competence

Confident, direct

There are key elements to writing a successful proposal

Your proposal must have a high likelihood of producing results that will have an impact:
— ***Emphasize Significance, Innovation!***

Your proposal must be easy to understand:
— ***Keep it simple, concise & logical!***

You must know what is required for the proposal:
— ***Read the Instructions!***

You must know how the proposal will be reviewed:
— ***Write to the Review Criteria!***

Research questions must have significance and impact

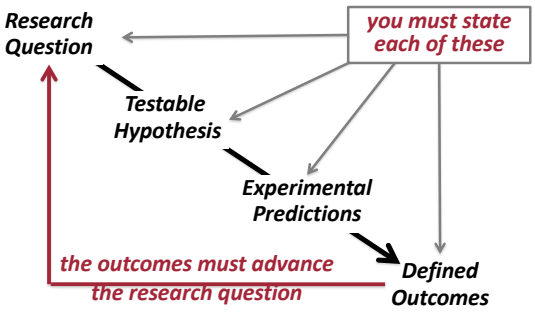
Does the project address an important problem?
A gap in knowledge or treatment?

If the goals of the project are achieved,

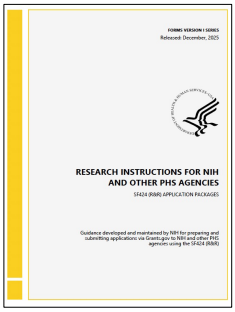
- how will scientific knowledge or clinical practice be improved?
- will the results ***exert a sustained, powerful influence on the research field?***

Floyd Bloom, MD

Your proposal must have a logical framework and tell a coherent story



Understand the instructions and write to the review criteria — *R Awards*



Significance **Factor 1**

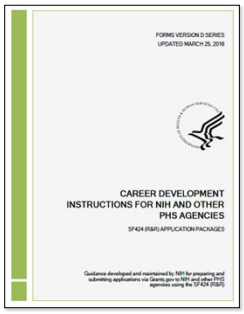
Innovation

Approach **Factor 2**

Investigators **Factor 3**

Environment

Understand the instructions and write to the review criteria — *K Awards*



Candidate

Career Plan

Research Plan

Mentors

Environment

The power of narrative . . .

Which is more persuasive?

https://www.flickr.com/photos/vipnyc/2620302548

Narratives have . . .

Actors

Action

Structure

Writing Science in Plain English
Anne E. Greene

Tell a good story . . .

Your audience will be convinced by your evidence but excited by your narrative . . .

Narratives have three parts:

1. **Set-Up** (exposition)
   — *the problem or question*
2. **Conflict/Action**
   — *how you will solve that problem*
3. **Resolution**
   — *the outcome you expect*

PAR Statement

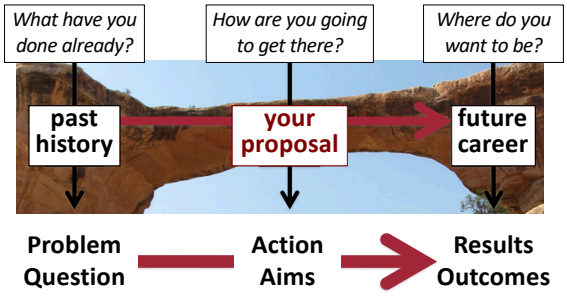
Problem → Action → Result

The Specific Aims page defines your narrative

A research proposal has narrative structure

Problem Question — **Action Aims** → **Results Outcomes**

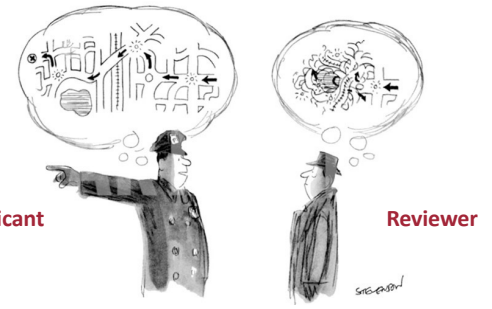
For a K Award the narrative is about YOU



Problem Question — **Action Aims** → **Results Outcomes**

Avoid the Curse of Knowledge*

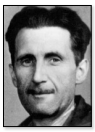
— the reviewer doesn't know what you know



*Steven Pinker *Sense of Style*

John Stevenson New Yorker Cartoon
February 16, 1976

Write simply, clearly, and logically



Apply George Orwell's rules for writing well . . .

Never use a long word where a short one will do.

If it is possible to cut a word out, always cut it out.

Never use the passive where you can use the active.

Break any of these rules sooner than say anything outright barbarous.

Politics and the English Language, Orwell, 1945
(https://biblio.wiki/wiki/Politics_and_the_English_Language)
Image: George Orwell's press card: http://www.netcharles.com/orwell/

If it is possible to cut a word out, always cut it out

Most **adjectives** and **adverbs** are unnecessary
— cut them out!

Delete the **"wiggle"** words:
— *a number of* (some, several)
— *in order to* (to)
— *is able to* (can)

Remove **excess modifiers:**
— *quite, totally, completely, absolutely*

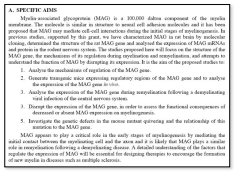
Avoid **redundancies:**
— *(knowledgeable)* experts
— *(new)* innovation

The Specific Aims page is the most important part of your proposal . . .

Describes concisely the goals, objectives & outcomes of the proposed studies

Is a useful summary for obtaining early feedback on your proposal *(reality check!)*

Is the hardest part of the proposal to write



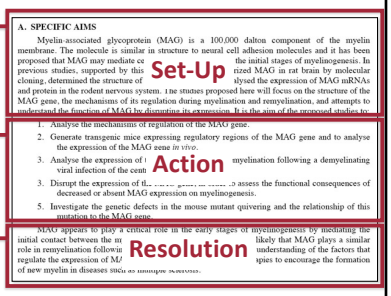
You must devote time to draft & polish your Specific Aims!

A good format for a Specific Aims Page is a sandwich

First paragraph
topic, goals, objectives, hypothesis, rationale

Specific Aims
objectives, description

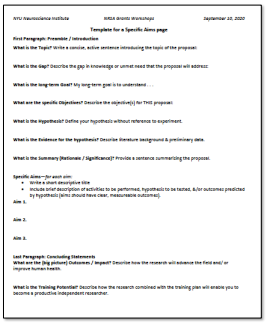
Last paragraph
impact, outcomes



Using the Template for a Specific Aims Page . . .

The Template lists the essential elements of a Specific Aims page

— complete each element as a sentence
— combine the sentences into a narrative
— polish
— review
— polish again
— ask for feedback
— polish again



The first paragraph provides the rationale for the proposed studies

What is the **Topic**?

What is the **Gap** in knowledge?

What is the long-term **Goal** of your research?

What are the specific **Objectives** for the proposal?

What is the **Hypothesis**?

What is the **Evidence** for the hypothesis?

What is the **Summary?**

You have a half page or less (~300 words) to set the stage for the proposal & excite the reviewer!

You must grab the reviewer's attention at the start —*consider opening lines in fiction . . .*

"It is a truth universally acknowledged, that a single man in possession of a good fortune, must be in want of a wife." Jane Austin *Pride and Prejudice*

"It was a bright cold day in April, and the clocks were striking thirteen." George Orwell *Nineteen Eighty-Four*

"We were somewhere around Barstow on the edge of the desert when the drugs began to take hold." Hunter Thompson *Fear and Loathing in Las Vegas*

"124 was spiteful." Toni Morrison *Beloved*

Compare with . . .

"It was a dark and stormy night; the rain fell in torrents, except at occasional intervals, when it was checked by a violent gust of wind which swept up the streets (for it is in London that our scene lies), rattling along the house-tops, and fiercely agitating the scanty flame of the lamps that struggled against the darkness."

Edward George Bulwer-Lytton, *Paul Clifford* (1830)

Start the Specific Aims with a concise, active statement introducing the topic of the proposal

Infantile Respiratory Virus (IRV) is a new agent that causes rapid inflammation of the lungs in young children.

Pancreatic cancer is commonly diagnosed only at an advanced stage.

Dysfunction of small vessels of the brain is associated with early cognitive impairment in dementias.

Your turn:

Compose a topic sentence for your proposal.

Next describe the gap in knowledge or unmet need that your proposal will address

But the exact mechanism of its pathogenesis is unknown, providing little guidance for treatment.

The lack of biomarkers for early-stage detection challenges effective treatment of this deadly cancer.

Vascular damage is usually ascribed to accumulation of amyloid-β but recent evidence implicates early changes in the blood brain barrier (BBB).

Your turn:

Describe the gap in knowledge or unmet need that your proposal addresses.

Describe the long-term goal of your research

The long term goal of our laboratory is to understand the biology of infectious agents to provide a foundation for effective therapies.

Our laboratory focuses on micro-RNAs (miRNAs) in the detection and treatment of cancers.

Our goal is to study the function and dysfunction of the BBB in dementias.

Your turn:

Describe the long term goal of your project.

For K Awards, describe your long-term career goals

My goal is to understand the biology of viral agents for leading a research program developing novel therapies for infectious disease.

My career goal is to be an independent investigator addressing the detection and treatment of cancers.

My long term career goal is to establish a research program investigating the mechanisms of dementia.

Your turn:

Describe the long term goal of your project.

Describe the specific objectives of your project

The objective of this proposal will define the mechanism of virus binding to its host cells in order to understand the pathogenesis of IRV.

The objectives of this proposal are to develop biomarkers for early detection of pancreatic cancer by investigating the expression of miRNAs.

In this proposal I will investigate the action of a novel factor — AFF1 — secreted by astrocytes on the BBB.

Your turn:

Describe the specific objectives of your project.

Define the hypothesis underlying your proposal

We will test the hypothesis that IRV initiates infection by binding of the IRV-knob protein to the CAR protein.

Our hypothesis is that tumorigenesis changes the expression of cellular and secreted miRNAs.

We hypothesize that inflammation of astrocytes stimulates release of AFF1 from astrocytic endfeet resulting in breakdown of the BBB.

Your turn:

Define the hypothesis for your project.

Describe the evidence for the hypothesis

Preliminary studies have shown that IRV can infect CAR-positive host cells but not CAR-negative cells.

We have shown that miRNA-179A and miRNA-208D are increased in expression in pancreatic tumor cells compared to normal tissue.

AFF1 was identified in a screen for genes upregulated in astrocytes following inflammation; knockout mice for AFF1 showed a decrease in BBB breakdown after an inflammatory stimulus.

Your turn:

Define the evidence for your hypothesis.

Provide a Summary for the proposal

The expertise of our laboratory on adenoviruses will be applied to the pathogenesis of a novel virus.

We will apply our extensive experience with miRNAs to the diagnosis of a common and highly lethal cancer.

This proposal will investigate the mechanism of action of AFF1 in vitro.

Your turn:

Define the rationale for your project.

Your Specific Aims should fit the scope of your effort

Fit the aims to the effort:

- R award — 3 aims
- K Award: one person (you!) over 3–5 years

Avoid contingent aims (the "fatal flaw")

Provide a timeline for your aims in the proposal

Aim	Year 1	Year 2	Year 3	Year 4
1	→			
2		→		
3			→	

First define the scope of your aims

1. To characterize the regions of the IRV-knob protein necessary for binding to the host cell CAR protein.
2. To develop monoclonal antibodies against regions of the IRV-knob protein that inhibit binding to CAR.

First define the scope of your aims

1. To characterize the expression of miRNA-179A and miRNA-208D in pancreatic tumor cells.
2. To determine the relationship between expression of miRNA-179A and miRNA-208D and pancreatic tumorigenesis.

First define the scope of your aims

1. To characterize the release of AFF1 from astrocytes in vitro.
2. To determine the action of AFF1 in astrocyte-capillary co-cultures.

Expand each specific aim to provide a short descriptive title & brief description

Aim 2. To determine the regions of the IRV-knob protein necessary for binding to the host CAR protein.

Our hypothesis predicts that alteration of the env region of the knob protein will decrease binding to the host cell CAR protein. We will test this prediction by

a) Generating variants of the knob protein with structural alterations in env.

b) Assessing binding to the CAR protein in vitro.

Your turn:

Write a title & description for a specific aim.

The last paragraph focuses on impact and outcomes

Outcomes & Impact :

These will define the mechanism of IRV infection and provide a foundation for immune therapy.

Development of biomarkers for early detection will result in dramatic improvement in the survival rate for pancreatic cancer.

These studies will characterize the function of a new factor with implications for the pathogenesis of dementias.

Your turn:

Describe the outcomes & impact of your project.

For K Awards, you should end with a statement about your career development

With the support of experienced mentors and additional training, this K award will enable the achievement of my goal to be an independent investigator conducting research in the field of . . .

infectious disease

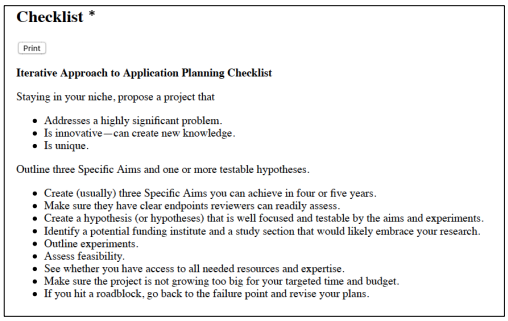
cancer research

neurodegeneration

Your turn:

Define the rationale for your project.

Next steps: put the elements into a coherent & logical narrative, polish, and get feedback



Checklist *

Print

Iterative Approach to Application Planning Checklist

Staying in your niche, propose a project that

- Addresses a highly significant problem.
- Is innovative—can create new knowledge.
- Is unique.

Outline three Specific Aims and one or more testable hypotheses.

- Create (usually) three Specific Aims you can achieve in four or five years.
- Make sure they have clear endpoints reviewers can readily assess.
- Create a hypothesis (or hypotheses) that is well focused and testable by the aims and experiments.
- Identify a potential funding institute and a study section that would likely embrace your research.
- Outline experiments.
- Assess feasibility.
- See whether you have access to all needed resources and expertise.
- Make sure the project is not growing too big for your targeted time and budget.
- If you hit a roadblock, go back to the failure point and revise your plans.

*NIAID Grants Tutorials — Specific Aims:
https://www.niaid.nih.gov/grants-contracts/draft-specific-aims

Warning: NIH strongly discourages use of artificial intelligence in grant preparation

- Based on the policy that NIH expects applicants to propose original ideas
- NIH will employ methods to detect use of AI and will not consider applications that are substantially developed by AI to be original ideas
- Post-award detection of substantial AI use may result in loss of funding and referral for research misconduct
- Applicants are limited to 6 applications per year as PI or MPI

See: NOT-OD-25-132

Best solution: do NOT use AI in preparing grants!

Well written specific aims help you . . .

Sort out the logic of your proposal:

— how many aims

— dependence of aims on each other

— feasibility and scope

Get **early** feedback on your proposal

Talk with a Program Officer

Questions?