How to Write an NIH Proposal

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Where Do I Go for Help?

Hyperlinked “help” flowchart

Large-Scale Proposal Coordination

High-value, higher-complexity, interdisciplinary
Smaller Proposal Consultation

Help is available for proposals of all sizes.

Proposal Preparation Timeline

Not a bad idea to start six months ahead of time!
Reviewers Want to Know

Specific aims page is key. Reviewers ask themselves three questions...

- Are you solving something that is critical to solve?
- Are you solving it the right way?
- Are you the right person to do this work?

Build the Storyline

Logic flow goes from broad to narrower

- What is the problem?
- What has been done already to address the problem?
- What is the gap that remains?
- How do you propose to address this gap?
Build the Storyline

What does this look like in NIH submission? Specific aims page template

Example of NIH-Style Outline

Specific Aims Page (1 page limit)

- State what is the human health problem. Write a compelling first sentence.
- Summarize what has been done already to address this problem.
- Clearly articulate the gap that still exists.
- State how you propose to address this gap?
  - Can have overarching hypothesis at this point and put the word \textit{hypothesis} in bold italics.
  - May be appropriate to state technologies you plan to use, describe expertise to do a task, map past accomplishments to your proposed work, explain the biology further, state how your aims work together.
- State how this work is innovative.

Aim 1: List your concrete objective here in bold run-on header starting with strong verbs such as identify, quantify, establish, determine.
- Describe each aim in two to three sentences.
- Can have working hypothesis if needed (this must test hypothesis).
- Can be to preliminary data.
- Convey the why this work needs to be done and/or the what will be done.

Aim 2: List your concrete objective here in bold run-on header starting with strong verbs such as identify, quantify, establish, determine.
- Describe each aim in two to three sentences.
- Can have working hypothesis if needed (this must test hypothesis).
- Can be to preliminary data.
- Convey the why this work needs to be done and/or the what will be done.

Aim 3: List your concrete objective here in bold run-on header starting with strong verbs such as identify, quantify, establish, determine.
- Describe each aim in two to three sentences.
- Can have working hypothesis if needed (this must test hypothesis).
- Can be to preliminary data.
- Convey the why this work needs to be done and/or the what will be done.

End with final paragraph on the expected outcomes of the research. What will you deliver/enable when you are successful? Should be at least one outcome per specific aim but also a general outcome.

Build the Storyline

Specific aims page is critical. You must make a good first impression.

- State what is the human health problem. Write a compelling first sentence.
- Summarize what has been done already to address this problem.
- Clearly articulate the gap that still exists.
- State how you propose to address this gap?
  - Can have overarching hypothesis at this point and put the word \textit{hypothesis} in bold italics.
  - May be appropriate to state technologies you plan to use, describe expertise to do a task, map past accomplishments to your proposed work, explain the biology further, state how your aims work together.
  - State how this work is innovative.
Build the Storyline

Example storyline starts your specific aims page

What is the problem?
What has been done already to address this problem?
What is the gap that remains?
How do you propose to address this gap?

Specific Aims

Microscopy has emerged as one of the most powerful and informative ways to analyze cell-based high-throughput screening (HTS) samples in experiments designed to uncover novel drugs and drug targets. However, many diseases and biological pathways can be better studied in whole animals—particularly diseases that involve organ systems and multicellular interactions, such as metabolism and infection. The worm Caenorhabditis elegans is a well-established and effective model organism that can be robotically prepared and imaged, but existing image-analysis methods are insufficient for most assays. We propose to develop algorithms for the analysis of high-throughput C. elegans images, validating them in three specific experiments to identify chemicals to cure human infections and genetic regulators of host response to pathogens and fat metabolism. Novel computational tools for automated image analysis of C. elegans assays will make whole-animal screening possible for a variety of biological questions not approachable by cell-based assays. Building on our expertise in developing image processing and machine learning algorithms for high-throughput screening, and on our established collaborations with leaders in C. elegans research, we will...

Writing Your Aims

What you will accomplish, your approach, and impact. Two to four aims.

Aim 1: List your concrete objective here in bold run-on header starting with a strong verb
Describe each aim in one to three sentences.
• Can have working hypothesis if needed
• Can tie to preliminary data
• Convey the “why” this work needs to be done as well as the “what” will be done
Writing Your Aims

**Strong vs weak specific aim verbs**

**Weak:** Investigate, study, correlate, describe

**Strong:** identify, determine, define, establish, quantify

Weak tends to not have a definitive end point.

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**Writing Your Aims**

**What you will accomplish, your approach, and impact**

**Specific Aims**

Microscopy has emerged as one of the most powerful and informative ways to analyze cell-based high throughput screening (HTS) samples in experiments designed to uncover novel drugs and drug targets. However, many diseases and biological pathways can be better studied in whole animals—particularly diseases that involve organ systems and multicellular interactions, such as metabolism and infection. The worm Caenorhabditis elegans is a well-established and effective model organism that can be robotically prepared and imaged, but existing image-analysis methods are insufficient for most assays. We propose to develop algorithms for the analysis of high-throughput C. elegans images, validating them in three specific experiments to identify chemicals to cure human infections and genetic regulators of host response to pathogens and fat metabolism. Novel computational tools for automated image analysis of C. elegans assays will make whole animal screening possible for a variety of biological questions not approachable by cell-based assays. Building on our expertise in developing image processing and machine learning algorithms for high-throughput screening, and on our established collaborations with leaders in C. elegans research, we will:

**Aim 1:** Develop algorithms for C. elegans viability assays to identify modulators of pathogen infection. To identify individual worms in thousands of two-dimensional brightfield images of worm populations infected by **Microsporidia**, and measure viability based on worm body shape (live worms are curvy whereas dead worms are straight).

**Approach:** We will develop algorithms that use a probabilistic shape model of C. elegans learned from examples, enabling segmentation and body shape measurements even when worms touch or cross.

**Impact:** These algorithms will quantify a wide range of phenotypic descriptors detectable in individual worms, including body morphology as well as subtle variations in reporter signal levels.
Innovation and Impact

Summarize long-term impact at end of specific aims page

Carolina Wählby’s paragraph after her three specific aims:

In addition to discovering novel anti-infectives and genes involved in metabolism and pathogen resistance, this work will provide the C. elegans community with (a)......, (b)...., and (c)....

Specific Aims Page is the Master Plan

Provides a map of the rest of your proposal

• Significance  STORYLINE INTRO
• Innovation
• Approach
Significance Section Elaborates on Story

Storyline in specific aims serves as a preview.

Specific Aims Page is the Master Plan

Provides a map of the rest of your proposal

- Significance
- Innovation
- Approach

STORYLINE INTRO

CLOSING PARAGRAPH
Innovation and Impact

Summarize long-term impact at end of specific aims page

Carolina Wähly’s paragraph after specific aims:

Aim 3: Develop algorithms for gene expression pattern assays to identify regulators of the response of the C. elegans host to Staphylococcus aureus infection
Challenge: To map each worm to a reference and quantify changes in fluorescence localization patterns.
Approach: We will develop worm mapping algorithms and combine them with anatomical maps to extract atlas based measurements of staining patterns and localization. We will then use machine learning to distinguish morphological phenotypes of interest based on the extracted features.
Impact: These algorithms will enable addressing a variety of biological questions by measuring complex morphologies within individual worms.

In addition to discovering novel anti-infectives and genes involved in metabolism and pathogen resistance, this work will provide the C. elegans community with (a) a versatile, modular, open-source toolbox of algorithms readily usable by biologists to quantify a wide range of important high-throughput whole-organism assays, (b) a new framework for extracting morphological features from C. elegans populations for quantitative analysis of this organism, and (c) the capability to discover disease-related pathways, chemical probes, and drug targets in high-throughput screens relevant to a variety of diseases.

Primary collaborators

Specific Aims Page is the Master Plan

Provides a map of the rest of your proposal

• Significance  STORYLINE INTRO
• Innovation  CLOSING PARAGRAPH
• Approach  AIMS
Writing Your Aims

What you will accomplish, your approach, and impact

Aim 1: Develop algorithms for C. elegans viability assays to identify modulators of pathogen infection Challenge: To identify individual worms in thousands of two-dimensional brightfield images of worm populations infected by Microsporidia, and measure viability based on worm body shape (live worms are curvy whereas dead worms are straight). Approach: We will develop algorithms that use a probabilistic shape model of C. elegans learned from examples, enabling segmentation and body shape measurements even when worms touch or cross. Impact: These algorithms will quantify a wide range of phenotypic descriptors detectable in individual worms, including body morphology as well as subtle variations in reporter signal levels.

Significance

Your research must solve a critical problem

• write for a broad scientific audience
• Answers the “so what?” not the “how.” If your research works as proposed, will your results be important for the field?
• addressing the gap should be a natural extension of your research
Innovation

Not status quo but enabling a new direction to the research area

- innovation can be in your new theory or in your novel methods and tools
- best if you include both

Approach

Describes your experimental design

- Is your project workable as described?
- When you are done, will the results be clear?
- relate each specific aim back to your storyline and show how results will help address gap
Preliminary Data

Purpose is extension and feasibility

- naturally extends your existing research but not merely incremental advances
- assures reviewers that what you propose will be feasible

Two Options for Preliminary Data

Outline to be consistent in format for a well-structured approach section

Title of Specific Aim #1

Introduction to Approach

Justification and Feasibility
  - Review of relevant literature
  - Preliminary studies

Research Design
  - Expected Outcomes
  - Potential Problems and Alternative Strategies
Two Options for Preliminary Data

Outline to be consistent in format for a well-structured approach section

Preliminary Studies (for all the aims together)
Title of Specific Aim #1 (verbatim from your specific aims section)
   – Introductory paragraph

Research Design

Expected Outcomes

Potential Problems and Alternative Strategies

Internal Review

We can help find experienced reviewers to provide feedback

NIH Writing Timeline

[Diagram showing timeline with months, deadlines, and review stages]
Questions?

More about NIH

Perry Kirkham
Scientific Review

From submission through review

Scientific Review Officers

1. Center for Scientific Review
   - Standing study sections
   - Special Emphasis Panels

2. Internal IC reviews
   - Standing study sections
   - Special Emphasis Panels
Center for Scientific Review

**Twofold Mission:**

1. Assign proposals

**Receipt and referral –**

a. read as much of the proposal as necessary to make an appropriate assignment (suitability, IC, dual assignment, review)

b. consider the PI request

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Center for Scientific Review

**Twofold Mission:**

2. achieve optimal peer review

Peer Review – IRG (study section)

http://cms.csr.nih.gov/PeerReviewMeetings/CSRIRGDescriptionNew/

- CB – Cell Biology (IRG)
  - BDPE – biology and diseases of the posterior eye (SS)
  - NCSD – nuclear and cytoplasmic structure/function and dynamics (SS)
  - CMAD – cellular mechanisms in aging and development (SS)
  - CSRS – cellular signaling and regulatory systems (SS)
  - DEV1 – development 1 (SS)
  - DEV2 – development 2 (SS)
Assignment by CSR Receipt and Referral

Solicited

RFA

PA

Assigned to persons prescribed in FOA

Unsolicited

Program

Institute

IRG

Program Officer

Scientific Review Officer

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Part 2. Full Text of Announcement
Section I. Funding Opportunity Description

The Center for Scientific Review (CSR) is the portal for NIH grant applications and their review for scientific merit. We receive all research grant applications sent to NIH and handle the review of more than 70% of those by organizing peer review groups (study sections) to evaluate research grant applications. Our mission is to see that NIH grant applications receive fair, independent, expert, and timely reviews – free from inappropriate influences – so NIH can fund the most promising research.

Find a Study Section

Applications are reviewed in Study Sections (Scientific Review Group, SRG). Integrated Review Groups (IRGs) are clusters of Study Sections based on scientific discipline.

Search Integrated Review Group (IRG) / Study Group

Tools and guidance for the successful reviewing, critiquing and scoring of applications.

Tools developed for NIH staff to access Meeting Status and PAR Tables to share.

CSR Newsletter

To keep informed about CSR activities and plans, please subscribe to our Listserv.

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More
Center for Scientific Review

Study Section

BDPE
http://cms.csr.nih.gov/PeerReviewMeetings/CSRIRGDescriptionNew/CBIRG/BDPE.htm

Topics covered
Membership roster (standing members) **
Meeting roster (reviewers for a specific meeting)
SRA (SRO)
Study sections with areas of similar science

Scientific Review

Choosing a study section

Not always necessary
If desired, do your homework well!
   CSR website – look for keywords
   RePorter – look for keywords
      look for topics
      look for colleagues
What are they looking for?
Response to Scientific Review

Summary Statement

Who is the program officer?
What are the salient points?
Who made the salient points?
Which of those can you address easily?
Which must you address?
What do you do if you disagree?
What is not in the text?
What is the “tenor” of the discussion
Response to Scientific Review

What next?

Go forward with a revision?
Go forward with a new application?
Revise but request a different study section?
Write a new application using the same study section?

Office of Proposal Development  Tufts University  9/15/2010

“It was generally seen that integrating preliminary data with the appropriate aim was an effective approach. Both too little preliminary data and too much preliminary data were seen as ineffective. "Shortchanging" preliminary data hurt scores, particularly if the data were relevant to the innovation. Even with published data, including enough context is key. The proposal should be able to stand on its own, and the burden is on the applicant to make certain that there is enough information for the reviewers.”

“The most consistently effective strategy for the Approach was to treat each aim like a story. These proposals integrated necessary background information and preliminary data into the approach for each aim.:

“Some investigators chose to "save space" by not using any figures. This was considered a major failing. Lack of figures or tables and lack of white space indicated that the grant writer was having difficulty adapting to the new format, and this approach was not viewed favorably.”