BRIGHAM AND WOMEN'S HOSPITAL

CENTER FOR Faculty Development & Diversity

Sharing strategies. Supporting careers.

Insights for Investigators Series:

Grant Writing Tips & Strategies for NIH R01s

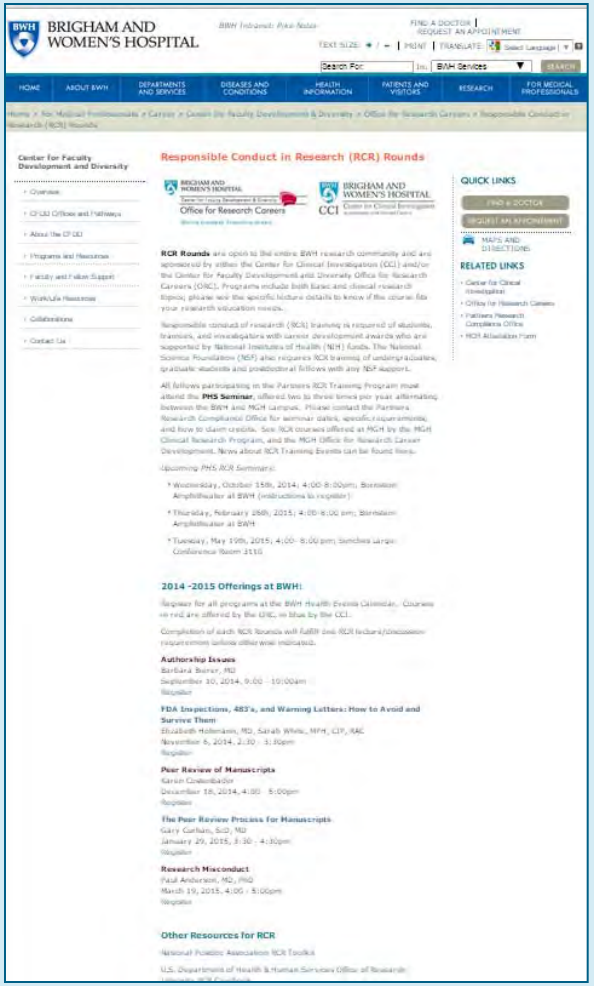
Robert C. Fuhlbrigge, MD, PhD

December 3, 2015

Responsible Conduct of Research

BWH RCR Website:
www.brighamandwomens.org/research/RCR

These case-based discussions provide a forum for researchers to examine the complicated and challenging issues which can arise in professional life and meet the NIH's RCR requirements.



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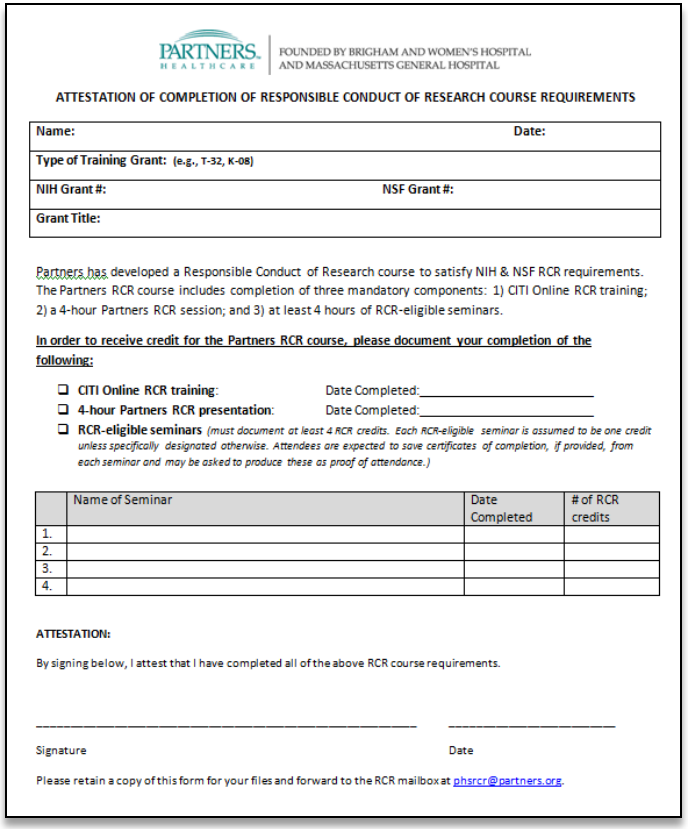
Center for Faculty Development & Diversity(CFDD) and **Center for Clinical Investigation (CCI)**

Responsible Conduct of Research

RESPONSIBLE CONDUCT OF RESEARCH (RCR) credit available

To obtain RCR credit:

1) **Complete your RCR Attestation Form;**
   1) **List seminars you have attended which have been designated for RCR eligible.**
2) **Email it to phsrcr@partners.org**
3) **Maintain your RCR Attestation Form for your own records for grant renewals.**



PARTNERS HEALTHCARE | FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL AND MASSACHUSETTS GENERAL HOSPITAL

ATTESTATION OF COMPLETION OF RESPONSIBLE CONDUCT OF RESEARCH COURSE REQUIREMENTS

Name:	**Date:**
Type of Training Grant: (e.g., T-32, K-08)	
NIH Grant #:	**NSF Grant #:**
Grant Title:	

Partners has developed a Responsible Conduct of Research course to satisfy NIH & NSF RCR requirements. The Partners RCR course includes completion of three mandatory components: 1) CITI Online RCR training; 2) a 4-hour Partners RCR session; and 3) at least 4 hours of RCR-eligible seminars.

In order to receive credit for the Partners RCR course, please document your completion of the following:

- ❑ **CITI Online RCR training**: Date Completed:_____
- ❑ **4-hour Partners RCR presentation**: Date Completed:_____
- ❑ **RCR-eligible seminars** *(must document at least 4 RCR credits. Each RCR-eligible seminar is assumed to be one credit unless specifically designated otherwise. Attendees are expected to save certificates of completion, if provided, from each seminar and may be asked to produce these as proof of attendance.)*

	Name of Seminar	Date Completed	# of RCR credits
1.			
2.			
3.			
4.			

ATTESTATION:

By signing below, I attest that I have completed all of the above RCR course requirements.

_____ _____

Signature Date

Please retain a copy of this form for your files and forward to the RCR mailbox at phsrcr@partners.org.

http://resadmin.partners.org/RM_Home/Research_Support_Depts/Research_Oversight/Partners_Research_Compliance/PHSResearchCompliance.aspx

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The Virtuous Cycle

Grants

Papers

Research

Grants

Money: How to get it

Grant tips and strategies

- Funding Sources
- Life Cycle of a Research Grant
- Developing a Strategic Approach
- The Specific Aims
- The Rest of the Story
- Resources on the Web

Funding Sources

- Foundations
  - Disease directed (ACS, NMSS, JDRF)
  - Investigator directed (HHMI)
  - Global Health (Gates Foundation)
- Federal agencies
  - National Institutes of Health (NIH)
  - National Science Foundation (NSF)
  - Patient Centered Outcomes Research Institute (PCORI)
- Industry (Big and Small)
  - Scientific Research Agreements, Contract service, licensing
- Philanthropy

NIH Funding Mechanisms:
Because that is where the money is

- R01 (investigator initiated)
- R21 (exploratory research grants)
- K series (mentored grant applications)
- U01/P01 (collaborative program projects)
- Program announcements (PA)
- Request for applications (RFAs)

comprehensive list of extramural grant and cooperative agreement activity codes

http://grants.nih.gov/grants/funding/ac_search_results.htm

Foundation funding mechanisms

- Highly variable
  - Organization specific
  - Changes from year to year
- Often low or zero overhead allowed
- Community of Science
  - PIVOT Database - comprehensive list of funding opportunities
  - Active search and email notification options
  - http://pivot.cos.com/about_pivot

Strategies for building a grant portfolio

- First grant (Oriented to early career development)
  - Foundations (Small/ pilot grants and CDA)
  - K awards
- Second grant (and 3rd, 4th, etc.) (Require a track record and preliminary data)
  - R01 awards
  - Foundation awards (research grants)
  - High-risk/ Pilot/ Planning grants: R03, R21, Others
- Mid-career grants
  - P01 (Multi-investigator: Collaboration around a specific area/topic)
  - U19 and P30 (Centers of excellence, technology cores, etc.)
- Industry
  - Investigator Initiated
  - Funding and reagents
  - Clinical Trials

LIFE CYCLE OF A RESEARCH PROPOSAL

- Develop a critical idea for a research proposal
  - Respond to:
    - Program Announcement (PA)
    - Request for Applications (RFA)
    - Investigator Initiated Grant
- Gather required materials
  - Access to key technologies/ materials, Preliminary data, collaborators
- Prepare and submit your proposal
- Repeat

Review Process for a Research Grant Application

PI Initiates Research Idea

Submits Application to NIH

Center for Scientific Review

Assign to IRG/ Study Section

Study Section

Review for Scientific Merit

Institute

Evaluate for Relevance

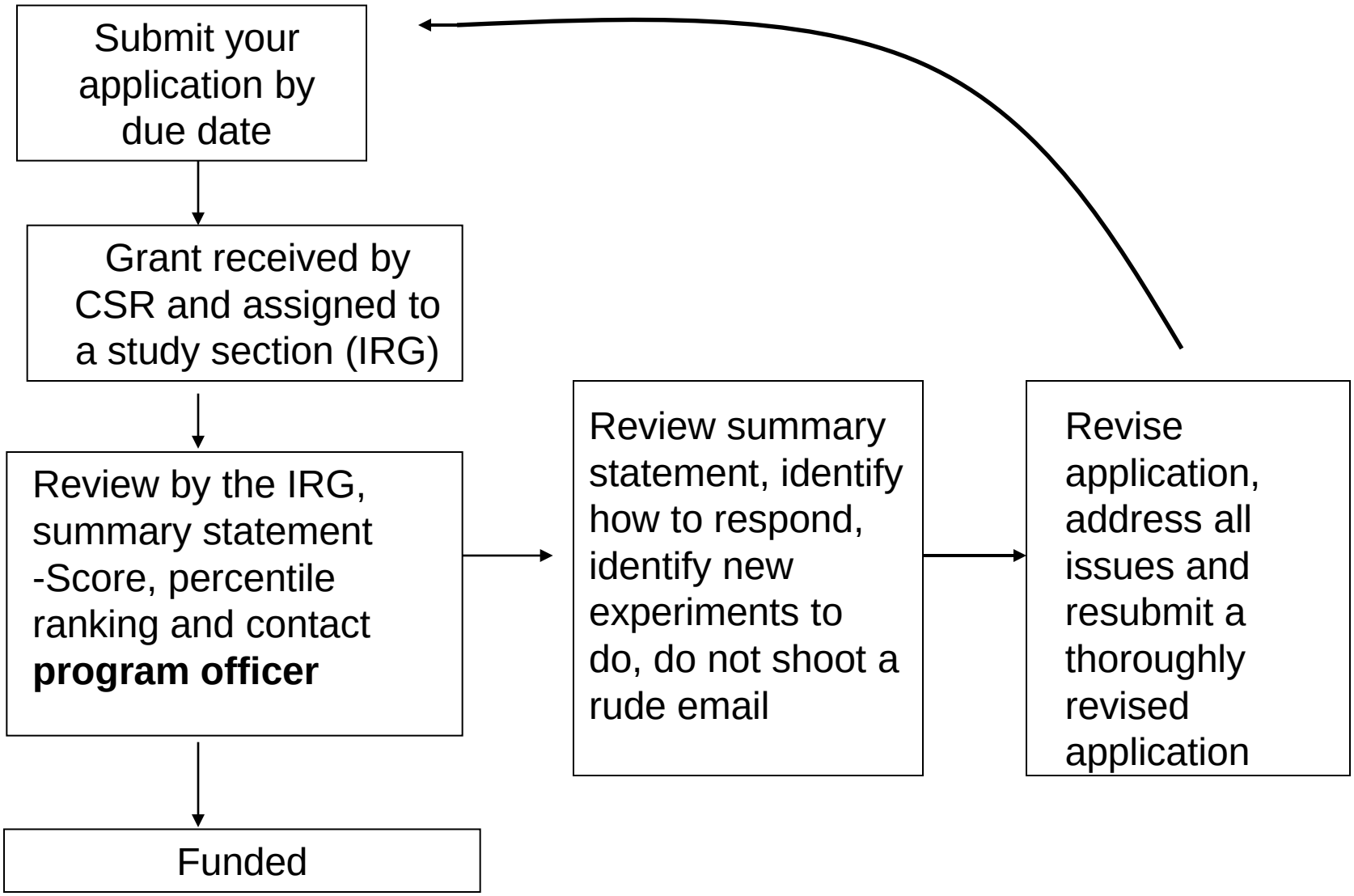
Advisory Councils and Boards

Recommends Action

Institute Director

Allocates Funds

From submission to funding



LIFE CYCLE OF AN NIH RESEARCH GRANT

Timing

- Submission dates: October, February, June
- Reviewed in Feb/March, June/July, Oct/Nov
- Goes to Institute advisory Council May/June, Sept/Oct, Jan/Feb
- Earliest award: July, December, April
  - 9 months from 1st submission
  - 15 months if revised and resubmitted immediately

PREPARING AN APPLICATION: Global issues

- read the instructions
- READ THE INSTRUCTIONS
- Read the CORRECT instructions, i.e., those pertaining to the grant for which you are applying (every grant application has an RFA/specific instruction set)
- Read ALL of the instructions and FOLLOW THE MOST CURRENT instructions

Organizing the application

- Identify/ clarify the idea
- Develop tools and technologies
- Recruit collaborators
- Generate preliminary data

continuous

- Write specific aims
- Discuss aims with a colleague
- Generate budget and administrative pages
- Prepare first draft of Research

6-12 weeks

- Give yourself plenty of time
- Discuss aims and the application with colleagues

- Draft all sections
- Obtain critique and discuss
- Submit draft with admin. pages for review

3 weeks BEFORE deadline

- Polish application
- Cross check budget, budget justification and time lines
- Check spelling, formatting
- Submit Final proposal

1 week BEFORE deadline

PREPARING AN APPLICATION: Local Issues

Grants administration

- Institution
  - Responsible for compliance with federal laws
    Human subjects, animal care, ethics, etc.
  - Responsible for submitting to funding agency
- Department/ Division
  - Responsible for budget and certification
    Hospital policies
    Salaries, subcontracts
  - Are required resources available (space, equipment, personnel)
  - Responsible for transmitting to Institutional RA
    Collection and confirmation of required documents/ signatures

IRB (Institutional Review Board)- Human subjects

IACUC (Institutional Animal Care and Use Committee)- Animal use

PREPARING AN APPLICATION: Local Issues

- Notify Dept./Div. with your plans to submit early as possible- at least two months in advance
  - Name and contact info (web-link) for sponsor/program
  - Date application is due
  - Special needs (subcontracts, special equipment, letters of support, special circumstances)
- Provisional administrative sections due a minimum of 3 weeks in advance
  - Key personnel
  - Provisional budget with details of subcontracts if needed
- Final proposal 1 week in advance (NEVER less than 3 days)
  - Remember you are not the only one submitting
  - Errors that result in stopping your proposal hurt you and not RA

Components of an RO1

- Administrative section
  - Key Personnel
    - Biosketches (NEW format)
    - Other support
  - Budget/ Budget Justification
  - Resources and Environment
  - IRB/ Animal protocol approval
  - Cover Letter- Identify preferred study section and Institute
- Scientific section
  - Abstract/ Narrative
  - Specific aims
  - Research plan
  - Human subjects
  - Vertebrate animals
  - Letters of support

SPECIFIC AIMS

- Arguably the **most important** part of the application
- Constitutes the template or master plan for your proposal
- The Specific Aims should include **EVERYTHING** that is important and exciting about your application- and **NOTHING** that is not important or exciting
- Will be used by the SRO to recruit/ assign reviewers
- Most members of the study section will ONLY read the Specific Aims before they vote a score

Most members of the study section will ONLY read the Specific Aims before they vote a score

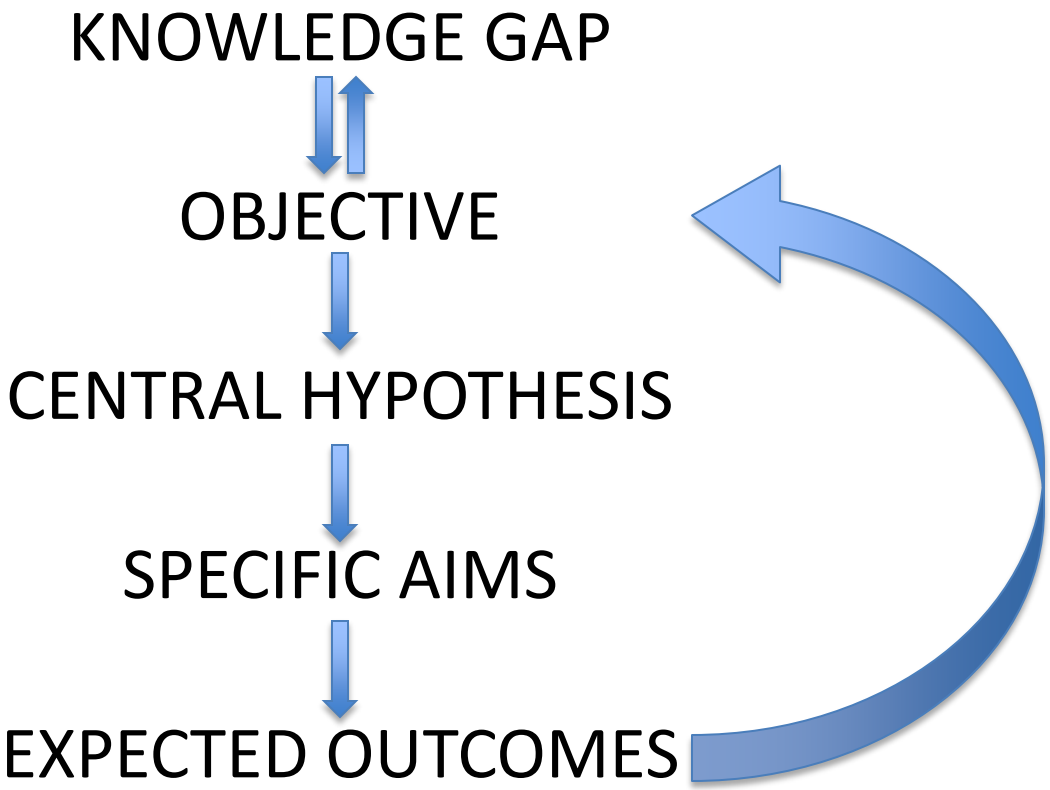
SPECIFIC AIMS

- The Specific Aims section should be written to create a partnership with the assigned reviewers
  - **You** provide the conceptual framework upon which the **Reviewers** hang the details of what will be done
- Reviewers (and non-reviewer panel members), in general, will have formed their general conclusion regarding your proposal by the end of the specific aims page
  - **Use the Specific Aims page to convert the reviewer into your advocate**

SPECIFIC AIMS: Key Components

- Introduction – Define the **Critical Need/ Knowledge Gap**
  - Identify a problem that MUST be solved (not just an interesting unknown you want to solve)
  - Must align with the mission of the funding agency
- Objective and Rationale - "**What, Why, Who**"
  - What is the Central Hypothesis
    - must be testable/ answer identifiable from experimental outcome
    - Should NOT confirm a predetermined conclusion
  - Why now and why you?
    - Unique opportunity, novel tools, specialized skills, key samples, etc.
- Aims – **Specific steps** to address the knowledge gap
- Significance - The "Payoff"
  - Novelty, Innovation, Expectations, Impact

SPECIFIC AIMS: The Logic



SPECIFIC AIMS: Introduction

- The **opening sentence** must grab the readers interest establishes the relevance of the proposal to human health
  - Tell the reviewer how supporting your proposal will help the NIH accomplish its goals

    e.g., http://provocativequestions.nci.nih.gov/
- A **statement of current knowledge** –do not assume expertise, help the reviewers get up to speed with what is known about the topic
- Introduce the missing link -What is the **gap in knowledge** that is holding back the field and that you will address in the application.

SPECIFIC AIMS: Opening Sentence

Lung Cancer is the leading cause of cancer deaths among both men and women in the U.S.

Obvious, non-focused, no idea what the grant is about

Failure to identify regional lymph node metastases in the 40,000 US patients/yr with surgically resected lung cancer is associated with a 3-fold increase in recurrence and a decrease in overall survival.

Focused, adds information, identifies a problem and relates to the mission of the agency (NCI)

SPECIFIC AIMS: Objective and Rationale

- The **long term goal** - what is the "big picture?"
- The **objective-** link back to the gap in knowledge
  - You have the solution to the critical need
  - Emphasize the product and not the process
- The **central hypothesis** must link to the objective
  - Show how the objective **will be** accomplished by testing the central hypothesis
- The **rationale** conveys why
  - Why is this question important, what will it change?
  - Tell the reviewers what will become possible after the research is conducted that is not possible now!
  - Why are you (and your colleagues) the best team to address this question right now

SPECIFIC AIMS: The Aims

- The Aims are the CORE of any research proposal
  - Well-designed aims make creating the rest of the grant easier
- There must be complete concordance between the aims and your central hypothesis.
  - Relate the purpose of the proposal to the critical need (and mission of the funding agency)
- Brief, informative, headlines that will attract the reviewer's attention.
  - Each aim should convey **WHY** that part of the research is being done, not what will be done.

SPECIFIC AIMS

- Should **be brief**, focused, and limited in scope.
  - The key steps to fulfill the objectives and address the critical need
  - explain how each will inform/ **test the central hypothesis**
- Your aims MUST NOT
  - Be descriptive or non-committal: avoid words like “compare”, “describe”, “investigate,” “determine whether”
  - Be conditional: avoid having the feasibility of one aim depend on the result of another
- Your aims must **be realistic**:
  - do not overestimate your abilities or capabilities for completing the work proposed in the time requested
  - “Cure cancer” vs. “Improve the staging and treatment of resectable lung cancer”

SPECIFIC AIMS: Examples

This multi-institutional collaborative proposal presents a coherent plan to overcome the barriers to diagnosis and management of patients with early-stage cutaneous T-cell lymphoma (CTCL) by definitively establishing that high-throughput sequencing (HTS) can solve the 3 major clinical problems in the care of these patients.

Specific Aims

1. Evaluate the ability of HTS to provide superior diagnostic classification in patients with early stage CTCL
2. Evaluate the ability of HTS to stratify risk for progression
3. Evaluate the ability of HTS to accurately assess responses to therapy

SPECIFIC AIMS: Significance

- The final paragraph helps to develop advocacy for your proposal
  - Especially among the majority of reviewers who will not, in all likelihood, have read the complete application
  - Summarize the innovation and novelty
- Articulate the expected outcomes/ products of the research
  - What is the payoff (ROI) that will be realized by funding of your application
- Summarize the general impact of the expected outcomes.
  - A positive impact statement should make it clear that the outcomes will advance your field as well as contribute to the mission of the funding agency.

Engage the Reviewer

- Provide a figure
- Utilize color, **BOLD** and *Italic*
- Should be able to understand just by reading the highlighted text
- Leave white space

SPECIFIC AIMS: Summary

The Specific Aims focus the reviewer (and you) on the main points of the grant

- Introduction –
  - Opening sentence and identification of the Critical Need
  - Alignment with the mission of the funding agency
- Objective and Rationale
  - The hypothesis and your solution
- Specific Aims
  - Steps you will take to address the critical need
- Significance
  - Point out Novelty, Expectations, Impact

RESEARCH DESIGN: 'Expanded Aims'

The 'heart and soul' of the application. In this section, state precisely

- What you propose to do (restate aims)
- How you plan to do it
- What the results will mean in terms of the overall project (estate link to objectives)
- What pitfalls you might consider
- Alternative approaches to cope with the anticipated problems or pitfalls

Research Strategy (12 pages)

- Significance/ Rationale (Expanded from Aims)
  - Importance of the problem
  - How proposed studies will improve scientific knowledge
  - How concepts/methods will drive the field
- Innovation (MUST state specifically!)
  - Innovations, refinements or improvements
    - "The innovations in this proposal are…"
  - New methods, approaches or concepts
  - How application will change understanding in the field

Research Strategy

Approach

- Preliminary studies (for new applications)
- Progress report (for competitive renewal)
- Overall strategy and methods
- Analysis methods/ statistics plan
- Alternative strategies
- Pitfalls and Additional considerations

PRELIMINARY STUDIES

- New Applications
  - Progress report in renewal applications
- Describe published studies in limited detail and include only the most important figures and/or tables.
- Describe unpublished studies in more complete detail, including newer data.
- Do not duplicate the preliminary studies with the proposed studies.

RESEARCH DESIGN continued

List each Specific Aim and provide:

- Introduction: Restate hypothesis /objectives
- Detailed methods/ approach
- Anticipated findings or results
- Potential pitfalls/alternative approaches

Watch your words

- Clarity
- Content
- Coherence
- Cutting edge

- Be simple, precise and direct (60-100 applications reviewed per IRG meeting)
- Build interconnected aims directed to a single hypothesis
- Hypothesis driven - NOT a fishing expedition
- Keep it simple: Use only one or two systems
- Do not be sloppy (zero tolerance for spelling errors and formatting issues)!
- Give credit to others
  - Never hurts to cite members of the review panel as appropriate

Review Criteria

- Overall Impact
- Significance
- Investigator
- Innovation
- Approach
- Environment

Strengths and weaknesses

1= Exceptional
2= Outstanding
3 = Excellent
4 = Very Good
5 = Good
6 = Satisfactory
7 = Fair
8 = Marginal
9 = Poor

NRFC = Not recommended for further consideration
UN = Unscored

After all that, how could they NOT fund my proposal?

NIH budget is flat, Congress dysfunctional

Funding paylines 6-12%

In the end, there is no substitute for:

1. Good science
2. Productivity

Application Resources on the Web

http://funding.niaid.nih.gov/researchfunding/grant/pages/appsamples.aspx Examples of successful RO1s annotated with what is positive. A MUST READ.

http://sciencecareers.sciencemag.org/career_development/tools_resources /how_to_guides/how_to_get_funding AAAS very useful site. Read: How Not to Kill a Grant Application.

http://grants1.nih.gov/grants/grant_tips.htm Tip guide from NIH. Includes tips for new investigators and SBIR/STTR. All you wanted to know about NIH and were afraid to ask.

http://www.ninds.nih.gov/funding/grantwriting_mistakes.htm Five common mistakes in NIH grant applications.

Application Resources on the Web

- http://enhancing-peer-review.nih.gov/

  E*verything you need to know about the review criteria and scoring system*
- http://grants.nih.gov/grants/peer/reviewer_guidelines.htm
  Reviewer guidelines: Especially the section Overall Impact versus Significance
- http://cms.csr.nih.gov/ResourcesforApplicants

  Center for Scientific Review's resources for applicants
- http://cms.csr.nih.gov/ResourcesforApplicants/InsidetheNIHGrantReviewProcessVideo.htm

  CSR videos on peer review
- http://grants.nih.gov/grants/writing_application.htm

  OER's page on Writing Your Application
- http://www.nigms.nih.gov/Research/Application/Tips.htm

  25 Helpful Hints for New Investigators from NIGMS Staff
- http://deainfo.nci.nih.gov/extra/extdocs/gntapp.htm
  NCI's Short Guide to the Preparation of NIH Grant Applications
- http://funding.niaid.nih.gov/ncn/grants/default.htm

  NIAID 'All About Grants'