Preparing Competitive NIH Applications for Enhanced Peer Review

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grant writing wisdom
impact, impact, and impact
essence of success

NIAID Funding News,
November 12, 2009

Gets the point across …
Why the Enhancements?

• Engage the Best Reviewers
• Improve the Quality & Transparency of Review
• Ensure Balanced & Fair Reviews
• Continuous Review of Peer Review

Note they took care to say “Balanced & Fair” versus “Fair & Balanced” … main push for the reform was to reduce burden - to applicants, reviewers, and NIH - and shorten the time it takes good science to get funded
New Application Format

- 12-p research narrative for R01, Ks (candidate & research), R34, et al.
- All mechanisms shortened (e.g., R03, R13, R21, R36, Fellowships = 6 p)
- Research Strategy (single upload) addresses Significance, Innovation, & Approach
- Preliminary Studies become part of Approach
- Monitor notices in the NIH Guide & at Enhancing Peer Review (enhancing-peer-review.nih.gov)

Background & Significance, Preliminary Studies/Progress, and Research Design & Methods all become the Research Strategy – totally new for applicants and reviewers alike.
New Application Strategy

- Critical to know reviewers - study the study sections
- Narrowly focused study section - less emphasis on Significance needed
- Broad or not-the-best fit study section - more emphasis on Significance
- Impact and Innovation critical
- Need exciting, accessible, cohesive narrative to generate enthusiasm
- Spend more time on application strategy before writing

Many of these concepts are presented in more detail at NIAID: http://www.niaid.nih.gov/ncn/grants/cycle/part05.htm
Specific Aims

• Specific Aims remains the MOST important page of Research Plan (1 p limit)
• New focus on impact of results on the field
• SRG discussion of “Approach” limited, so this page sells grant (including study design) to non-assigned reviewers - may be the only page they read

Specific Aims is now officially it's own page in the new R01 narrative format - this advice holds true no matter the mechanism, sponsor, etc.
Specific Aims

• Creates focus for application
• Conveys big picture - impact, significance, innovation
• Conveys relevance to public health
• Explains why you chose the project
• Milestone-driven objectives that will provide useful data whether outcome is positive or negative

This one page must get across all the important points for your story - and grab the reviewers' attention
Specific Aims

• Pitfalls:
  – Lack of original or innovative idea
  – Too ambitious
  – Fishing expedition
  – Not measurable
  – Incremental advance in knowledge
  – Not achievable in time available
  – No significant impact (even if aims achieved) on the field
  – Too many aims (>1/y)

Mainly, the science must have a significant wow factor and convince the reviewers it will have a real impact on the field
Significance

- “Explain importance of problem or critical barrier to progress in field being addressed”
- “Explain how project will improve scientific knowledge, technical capability, and/or clinical practice”
- “Describe how concepts, methods, technologies, treatments, services, or preventive interventions that drive this field will be changed if proposed aims are achieved”

NIH description
Significance

• Establish Significance through review of published & unpublished data in field (including own)
• Identify gaps in current knowledge
• Justify hypotheses & approach
• Highlight success of your related grants & awareness of potential barriers-alternative approaches
• Clearly state public health implications
• Suggested length: 2-4 p (1-2 p)

The first page length suggestion is for 12-p applications, the latter for 6-p proposals. The background & significance becomes Significance in the single Research Strategy narrative (vs Research Plan of old)
Significance

- Pitfalls:
  - Inappropriate, incomplete, or haphazard use of literature
  - Limited rationale for proposal - no evidence that data obtained will be new or unique or fill gaps
  - Uncertainty regarding future direction or significance of results
  - Insufficient or missing discussion of relevant published literature (including alternative theories or approaches ... and important papers by study section members)

I don’t want to read a standard literature review here – needs to be commentary, interaction with the literature, engagement with the latest data, etc.
Innovation

• “Explain how application challenges and seeks to shift current research or clinical practice paradigms”
• “Describe any novel theoretical concepts, approaches, methodologies, instrumentation, or intervention(s) to be developed or used and any advantage gained”
• “Explain any refinements, improvements, or new applications”

NIH description
Innovation

- Significance is why the work is important to do
- Innovation is why the work is different from (better than) what has been done before
- Definition of innovation: a new device or process resulting from study & experimentation; the act of introducing something new
- How will research in your field change as a result of your work

The review criteria for Innovation have always been tricky to nail down …
Innovation

- Demonstrate the potential gains are not merely incremental
- Explain why concepts & methods are novel to one field or novel in a broad sense (or both)
- Summarize (sans detailed data) novel findings to be presented as preliminary results in Approach
- Focus on innovation in study design & outcomes
- Suggested length: 1/2-1 p (1/2 p)

The first page length suggestion is for 12-p applications, the latter for 6-p proposals.
Innovation

• Pitfalls:
  – No novelty in either methods or their application to problem
  – No measurable impact on biomedical research and/or clinical care
  – No “paradigm shift”
  – Too similar to other funded (check RePORTER) or published research

If you can describe how you will shift an existing paradigm, be sure to do so - spell everything out & give the reviewer talking points for discussion
Approach

- “Describe the overall strategy, methodology, and analyses to be used to accomplish specific aims”
- “Describe how data will be collected, analyzed, and interpreted”
- “Discuss potential problems, alternative strategies, and benchmarks for success”
- “Describe any strategy to establish feasibility & address management of any high-risk aspects of work”
Approach

- Research design must achieve Specific Aims
- Preliminary studies/data incorporated throughout to demonstrate experience with/success of methods & establish feasibility
- Shows the hypothesis can be readily & clearly tested
- Publication record is critical – shows if you can deliver

The Preliminary Studies section goes away in the new shorter format, but some preliminary data can (must!) be incorporated in the approach section … lay out the approach by specific aim and incorporate relevant preliminary data as appropriate (nothing that has been published - and no tiny figures!)
Approach

- Think of pathways research could take based on results (more so than experiments themselves)
- Highlight your work that is different & that you do it well
- Give more detail for unique or new methods - less detail for routine approaches (reference published methods)

Can’t all be – here is my hypothesis, here are the structured experiments I will conduct to collect data to prove my hypothesis etc. Too boring – what if real science occurs and something completely unexpected happens – wow!
Approach

- Anticipate problems & include Plan B - decision tree illustrating branching next steps
- Logical sequence & timetable
- Must include adequate data analysis - interpretation plan & statistical support
- Show how results will lead to future experiments & translation to clinical practice
- Progress Report at outset for renewals
- Suggested length: 6-9 p (3-4 p)

The first page length suggestion is for 12-p applications, the latter for 6-p proposals. For Type 2 applications, I suggest putting Progress Report data at the outset of the Approach section and, for Type 1 applications, integrating preliminary data with the methods.
Approach

• Pitfalls:
  – Diffuse, superficial, unfocused design
  – Methods do not test hypothesis or achieve specific aims
  – Lack of experience/publications in essential methodology
  – Unrealistic timeline
  – No difficulties anticipated, no solutions proposed
  – Inadequate attention to data analysis, interpretation, and/or application

With the shorter application format, reviewers will rely on journal peer review of preliminary data & methods
Investigators

• Biosketch still 4 pages but more NSF-like
• Education & training info and positions & honors as before
• Up to 15 publications (encouraged), e.g.:
  – 5 most recent
  – 5 best
  – 5 most related to application
  – Include NIH Manuscript Submission or PubMed Central reference number as appropriate
• Research support for ongoing or projects completed within last 3 y

Keep the training info and positions & honors … personal statement is akin to Synergistic Activities on NSF biosketch
Investigators

• Personal statement about experience & qualifications
• Why you are the best person to do this research
• Focus on relevance to your role on current application
  – PI: prior success in field, manage independent research program, mentor trainees, etc.
  – Co-investigator: specific expertise, prior collaborations, etc.
  – Faculty/mentor: trainee history (# & level, % in academics, etc.)

You must sell yourself - this is the second review criteria so will be discussed at study section
Environment

- Resources (PHS398) or Facilities & Other Resources (item 9, SF424)
- How scientific environment in which research done will contribute to success – especially unique facilities, equipment, or populations
- ESI describe institutional investment (start-up package), mentorship, training, etc.
- Special facilities for biohazards (covered in Select Agent Research as appropriate)

If you have a CTSA, a special IC at your institution, etc., cite these … ESI doesn’t list $ amounts but refers to protected time, postdoc or technician/CRC, equipment, etc.
NIH Peer Review

• Read review criteria for each FOA carefully (Section V)

• Reviewer instructions available:
  grants.nih.gov/grants/peer/reviewer_guidelines.htm
  enhancing-peer-review.nih.gov/scoring_and_critique_overview_June2009.pdf
  cms.csr.nih.gov/PeerReviewMeetings/ReviewerGuidelines/

• Critique template available:
  grants.nih.gov/grants/peer/critiques/rpg_critique_template_example.doc

CSR is also where you will research study section rosters and foci
NIH Peer Review

• Overall Impact
• “Assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved”
• Impact Score only provided for discussed applications
• SRG discussions focus on impact

NIH charge to reviewers in assessing impact
NIH Peer Review

• 9-point scoring system also used to score individual review criteria (lower scores better)
• Review criteria scores are not weighted & are NOT used to calculate or otherwise determine Impact Score
• Can have high individual criteria scores but low Impact Score (and vice versa)
• Criteria scores not discussed at SRG – emphasis on impact

credit NIAID for best of breed analogy
The descriptors have meaning beyond ego inflation … “Exceptional” is new, which throws off a lot of seasoned PIs (“outstanding” used to be the best descriptor)
<table>
<thead>
<tr>
<th>Score</th>
<th>Descriptor</th>
<th>Additional Guidance on Strengths/Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Exceptional</td>
<td>Exceptionally strong with essentially no weaknesses</td>
</tr>
<tr>
<td>2</td>
<td>Outstanding</td>
<td>Extremely strong with negligible weaknesses</td>
</tr>
<tr>
<td>3</td>
<td>Excellent</td>
<td>Very strong with only some minor weaknesses</td>
</tr>
<tr>
<td>4</td>
<td>Very Good</td>
<td>Strong but with numerous minor weaknesses</td>
</tr>
<tr>
<td>5</td>
<td>Good</td>
<td>Strong but with at least one moderate weakness</td>
</tr>
<tr>
<td>6</td>
<td>Satisfactory</td>
<td>Some strengths but also some moderate weaknesses</td>
</tr>
<tr>
<td>7</td>
<td>Fair</td>
<td>Some strengths but with at least one major weakness</td>
</tr>
<tr>
<td>8</td>
<td>Marginal</td>
<td>A few strengths and a few major weaknesses</td>
</tr>
<tr>
<td>9</td>
<td>Poor</td>
<td>Very few strengths and numerous major weaknesses</td>
</tr>
</tbody>
</table>

**Minor Weakness**: An easily addressable weakness that does not substantially lessen impact

**Moderate Weakness**: A weakness that lessens impact

**Major Weakness**: A weakness that severely limits impact

There are several files explaining the review process for each mechanism that you can find at both CSR and Enhancing Peer Review.
NIH Peer Review

- Equation to convert new 10-90 scale impact scores to former 100-500 scale priority scores

$$5 \times (\text{New impact score} - 10) + 100 = \text{Old priority score}$$

5 \times (10 - 10) + 100 = 100
5 \times (20 - 10) + 100 = 150
5 \times (30 - 10) + 100 = 200
5 \times (40 - 10) + 100 = 250

On the descriptors, don't forget an extra adjective was inserted at the top (Exceptional), such that Outstanding now takes you to the bubble, with Excellent a bit farther out of funding reach (at least in current funding climate)
NIH Peer Review

- Equation to take into account instructions to use entire scoring range
- $3.5 \times (\text{New impact score} - 10) + 100 = \text{Old priority score}$

\[
\begin{align*}
3.5 \times (10 - 10) + 100 &= 100 \\
3.5 \times (20 - 10) + 100 &= 135 \\
3.5 \times (30 - 10) + 100 &= 170 \\
3.5 \times (40 - 10) + 100 &= 205 \\
3.5 \times (50 - 10) + 100 &= 240
\end{align*}
\]

Also better matches former descriptors (Outstanding, Excellent, etc.)
Comparison of Percentile vs Score for Old (5-pt) and New (9-pt) Scoring Systems (NIGMS R01 data, ~300 apps/figure)

From a Toni Scarpa presentation earlier this year - 1st round of 9-pt scoring
Another Toni Scarpa slide
Responding to Peer Review

- Scores = Significance, Investigators, Innovation, Approach, Environment
- Criteria discussed in order @ SRG
- Impact score = 22
- Percentile = 10
- Criteria scores =
  - 1, 1, 3, 2, 1
  - 2, 1, 3, 3, 1
  - 3, 2, 5, 2, 2
  - 2, 5, 5, 7, 2
  - 2, 2, 3, 2, 3

Numbers from an actual summary statement for an application that should be funded – note the range of criteria scores, most of which are higher than the impact score
FY10 Paylines – New Scores

- Most ICs do not post paylines
- NIAID - 8th/13th (R01), 24 for SBIR (NIAID will post detailed payline list when established)
- NIAMS - 13th/18th (R01), 13th (R21)
  
  28 for R03s  
  25 for R15s  
  25 for K01/K02/K08/K25s  
  25 for K23/K24s  
  14 for K99s  
  27 for F31/F32/F33s

NIAID provides the best payline coverage - but they will post no payline before its time
FY10 Paylines – New Scores

• NHLBI percentiles by amendment status toward funding >60% of R01s as A0
• NHLBI eliminated NI status - only ESI get 5-percentile break
• Other ICs likely to follow suit in both trends
• 16th (A0), 12th (A1), 10th (A2)

  16th percentile for R21s
  25 for P01
  35 for for P01 project

NHLBI made several policy changes all at once with little advanced warning
FY10 Paylines – New Scores

- NINDS - 13th (up to 16th for A0s, up to 23rd for High Program Priority)
- NLM - ≤30 for experienced PIs, ≤45 for new/ESI PIs (R01), ≤45 for K99
- NIA - 8th/13th (R01, may go above 13th for ESI PIs)

NLM usually funds at a higher payline - smaller pool of qualified applicants, interests
Responding to Peer Review

• Write what you really think - then run it through the shredder
• Do it again if necessary
• Do NOT get into a pissing match with reviewers
• Regard the summary statement as a valuable resource
• Response to prior review receiving less attention now – goal is to fund more A0s than A1s

Oh no - the reviewers “didn’t get it” the first time in … be sure to remember this when the time comes …
Responding to Peer Review

- Assume the reviewers are right
- Assume the comments are intended to be helpful
- Assume they all read the same application
- Assume more flaws exist in the application than are cited in the summary statement (especially with abbreviated bulleted comments)

The new summary statements in particular offer only cryptic comments on how/what to change/improve - do NOT assume addressing them is the end of your revision work!
Responding to Peer Review

• If a reviewer is wrong in a stated criticism, the problem is most likely with the application:
  – Lack of clarity in expressing idea
  – Poor writing or organization
  – Insufficient detail
  – Missing or incorrect figures or tables

Use the insight of what others miss or overlook to improve your next submission (whether an amended or new application).
Responding to Peer Review

- Most Introductions now limited to 1 page
- If space permits, quote concerns verbatim
- Start with concerns cited in the Resume & Summary of Discussion (if discussed) - these are the most important comments
- As space permits, group remaining concerns by Critique #

Never put words in the reviewers’ mouths - and never ignore comments, including the ones that make no sense (or show the reviewer did not read the application)
Application Timing

- Only one resubmission
- Submit best application rather than "get something in" & wait for reviewer feedback
- Can you readily fix the issues raised?
- Do you have compelling new data?
- Do you have additional manuscripts submitted or in press?
- Is the application stronger and more compelling/exciting and ready for resubmission?

Getting back to the NIH enhanced peer review …
## Application Timing

<table>
<thead>
<tr>
<th>New R01 Application Timing</th>
<th>Characteristics and Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review Cycle 1</td>
<td>• The cycle allows you to resubmit within the same fiscal year for review cycle 3.</td>
</tr>
<tr>
<td>Apply February 5, 2010</td>
<td>• Your application will be reviewed by the Council in September 2010.</td>
</tr>
<tr>
<td>(AIDS: May 7)</td>
<td>• You may experience a delay in your funding while we don’t have a budget or NIAID Payline. We have a limited number of grants to fund.</td>
</tr>
<tr>
<td>Council in September 2010.</td>
<td>• If your application is deferred – in the gray zone – for possible funding at the end of the fiscal year, you have the longest wait. Consider revising for cycle 3 instead of waiting.</td>
</tr>
</tbody>
</table>

| Review Cycle 2              | • When you get your score in October or November 2010, you may have an interim NIAID Payline but not an actual payline. |
| Apply June 7, 2010          | • You’re likely to experience the long delay for funding we described above. |
| (AIDS: September 7)        | • The earliest you could resubmit would be for review cycle 1 of the next fiscal year, which means your application would be funded under the next year’s payline. That could mean a long wait. |
| Council in February 2011.  | • The earliest you could resubmit would be for review cycle 2 of the next fiscal year, which means your application would be funded under the next year’s payline. |

Submit the application when it is ready

http://funding.nih.gov/newsletters/2009/1209.html#02

Prior to resubmitting, ask yourself: can you quickly fix the issues raised, do you have compelling new data, do you have additional manuscripts submitted or in press, etc. These latter questions apply to anyone deciding how soon to submit an amended application: is the application stronger and more compelling/exciting and ready for resubmission? Since it’s your last shot now, the answers all must be yes, or you should wait. The timing in terms of review cycle for new and amended applications should take this table into consideration - but not be driven by it.
Comments from Peers

- Apps discussed in order of preliminary scores, stopping when about 40% of apps discussed or time runs out
- Measure of competence based largely on track record
- “… given the paucity of material in the critiques, I am off to Madame Zelda to help me read the tea leaves - I might be able to expense that somehow”

Comments paraphrased from MWEG
Comments from Peers

- Be prepared for the correlation between score & percentile to vary quite a bit for the first few rounds [NIH staff]
- “No one knows how this will affect peer review” [NIH staff on shorter application length]
- Survey of peer review changes among 4,710 reviewers & applicants underway - survey responses due Jan 15, 2010

More from MWEG
Comments from NIH Director

- Do not expect better news for FY11, per Francis Collins:

  "... we have an economy that continues to struggle, we have a deficit that is now grown to something like $9 trillion. The scientific community should not in any way imagine that this [increasing NIH FY11 budget] is going to be easy."

Probably no more of an increase than has been received in recent years (ie. 1-2%) ... maybe even a cut?
NIH Grantsmanship Resources

- Medical Writing, Editing, & Grantsmanship
  - writedit.wordpress.com
  - writedit.wordpress.com/nih-paylines-resources/
- NIH Grant Cycle Explained & Grant Tutorials
  - www.niaid.nih.gov/ncn/grants/cycle/default.htm
  - www.niaid.nih.gov/ncn/grants/default.htm
- NIH Grant Basics
  - grants.nih.gov/grants/grant_basics.htm
- Clinical Research Toolbox
  - www.nia.nih.gov/ResearchInformation/CTtoolbox/
- Changes in peer review/applications
  - enhancing-peer-review.nih.gov/
  - grants.nih.gov/grants/peer/reviewer_guidelines.htm

NIAID has, hands down, the best grantsmanship resources on the Web ... look nowhere else for guidance, no matter “your” IC or specialty.