Learning from NIH Grant Summary Statements

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Learning from criticism

- Scoring system
- Failure modes in review
- The culture of summary statements
  - Applications meeting the payline (<10%ile)
  - Applications not discussed (>50%ile)
  - Examples of successes and failures
NIH Grant Summary Statements

Source material - Thousands of reviews

• Reviewers provide comments to individual grant applicants

• NIH program staff have access to confidential summary statements of many grant reviews

• Across all of medical research, grantsmanship errors are restricted to a few types

• Editing out the “science” shows this clearly

• Your funding depends on avoiding these errors
NIH Grant Summary Statements

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  o Applications meeting the payline (<10%ile)
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## Scoring System

<table>
<thead>
<tr>
<th>Impact</th>
<th>Score</th>
<th>Descriptor</th>
<th>Additional Guidance on Strengths/Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>1</td>
<td>Exceptional</td>
<td>Exceptionally strong with essentially no weaknesses</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Outstanding</td>
<td>Extremely strong with negligible weaknesses</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Excellent</td>
<td>Very strong with only some minor weaknesses</td>
</tr>
<tr>
<td>Medium</td>
<td>4</td>
<td>Very Good</td>
<td>Strong but with numerous minor weaknesses</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Good</td>
<td>Strong but with at least one moderate weakness</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Satisfactory</td>
<td>Some strengths but also some moderate weaknesses</td>
</tr>
<tr>
<td>Low</td>
<td>7</td>
<td>Fair</td>
<td>Some strengths but with at least one major weakness</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Marginal</td>
<td>A few strengths and a few major weaknesses</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Poor</td>
<td>Very few strengths and numerous major weaknesses</td>
</tr>
</tbody>
</table>
Scoring System

How a score is derived

- The study section discusses the top 50% grants
- Assigned reviewers state preliminary Impact Scores
- Each reviewer describes strengths and weaknesses
- These concerns are discussed by other members
- Final scores of assigned reviewers are stated
- The entire study section votes online by secret ballot
- The summary statement is compiled by the Scientific Review Officer using 3 written critiques, 2 of which include individual component scores for the 5 criteria
- Overall Impact score = (the mean of all votes) x10
- The scores are ranked in percentile for the study section
Scoring System

Summary statements consist of these sections

• Cover page with Impact score, data on application, and information on the study section meeting

• Resume and summary of discussion – Written by SRO

• Critique 1 – Review written by peer reviewer 1

• Critique 2 – Review written by peer reviewer 2

• Critique 3 – Some notes added by reviewer 3, the “reader”

• Administrative comments

• List of study section members and NIH staff
Scoring System

Summary statements contain several scores

- Significance
- Investigator(s)
- Innovation
- Approach
- Environment

Scores for each are given by both reviewers

- Other aspects affecting the overall impact score – Human subjects, inclusion of women, minorities and children, vertebrate animals, biohazards, select agents, resource sharing plans

- The overall impact score is not the arithmetic mean of the component scores from the written reviews
NIH Grant Summary Statements

Learning from criticism
  • Scoring system

  • **Failure modes in review**

  • The culture of summary statements
    o Applications meeting the payline (<10%ile)
    o Applications not discussed (>50%ile)
    o Examples of successes and failures
Failure Modes

• The engineering term “failure mode” applies to NIH grant reviews

• Reviewers frequently have concerns about the same, small number of grantsmanship issues, or failure modes

• Some concerns are straightforward to address, while others require a complete re-design of the project

• 6 failure modes are discussed here
Failure Modes

**Little significance to the work**

- If successful the project will have no relevance to the practice of medicine or to the biology of disease

- The current thinking in the field would only be reinforced by this work

- The investigator presents ideas to specialists and assumes that other reviewers grasp their significance

- Catch-all significance is claimed with no evidence linking the expected results of the project to the broader field
Failure Modes

Project is not innovative

- Planned work will yield merely an incremental increase in knowledge

- No state-of-the-art concept or state-of-the-art technology is involved
Failure Modes

Unprepared principal investigator

• Application is poorly written and plans are hard to understand or seem illogical

• The application is too densely written and hard to read, with little white space on the page

• Figure legends are missing or illegible

• Investigator has misinterpreted a principal concept

• Important citations from the literature are lacking

• Essential collaborations are not established
Failure Modes

Methods are not feasible

- No demonstration of each proposed method, material, or animal in the investigator’s published work or in preliminary results

- No collaboration with expert(s) in this field

- Alternative methods are not considered

- Plans are proposed to obtain or prepare essential reagents in the future, as has been done in the past
Failure Modes

Strategy is faulty

• One specific aim depends on a positive result from another aim

• Expected results, caveats or alternative approaches are not described

• Research design is too ambitious to be carried out with the resources and time allowed

• Research design is unfocused or diffuse and not aimed at answering one question
Failure Modes

Specific Aims do not test a hypothesis

• No formal hypothesis is stated

• Plans are “merely descriptive”

• A descriptive, general hypothesis is proposed

• A specific aim or subaim is designed to gather information, not to test a specific hypothesis

• Descriptive analyses of exciting, novel phenomena are planned

• Please note that some NIH programs issue requests for applications on a particular topic that requires descriptive research
Failure Modes

Failure modes in summary statements

• These 6 failure modes can be seen among each of the extracts of summary statements of the unfunded applications we will discuss

• Investigators avoiding these problems have greater success in review

• We will first review comments provided to applicants that were awarded their grant
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  o Applications meeting the payline (<10%ile)
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Examples of critiques

- Applications meeting a payline of $\leq 10\%$ile
  - 1 new investigator, 2 junior faculty, & 2 senior faculty
- Applications not discussed ($>50\%$ile)
  - 1 new investigator and 4 senior faculty
- The following extracts of actual summary statements were stripped of all scientific and medical terms
- The percentile ranks are shown within a range to maintain investigator anonymity
- The positive(✔️) and negative(❌) reviewer comments highlight the strategies and the presentation of ideas
## Culture of Summary Statements

Examples of 5 funded and 5 unfunded applications

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Types of application</th>
<th>Percentile Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. New PI</td>
<td>Revised new</td>
<td>30-40%, 1-5%</td>
</tr>
<tr>
<td>2. Jr. faculty</td>
<td>Competitive renewal</td>
<td>12-20%, 1-5%</td>
</tr>
<tr>
<td>3. Jr. faculty</td>
<td>Revised new</td>
<td>10-15%, 5-10%</td>
</tr>
<tr>
<td>4. Sr. faculty</td>
<td>Revised new</td>
<td>20-30%, 1-5%</td>
</tr>
<tr>
<td>5. Sr. faculty</td>
<td>Competitive renewal</td>
<td>30-40%, 5-10%</td>
</tr>
<tr>
<td>6. New PI</td>
<td>New</td>
<td>Not discussed</td>
</tr>
<tr>
<td>7. Jr. faculty</td>
<td>New</td>
<td>30-40%</td>
</tr>
<tr>
<td>8. Sr. faculty</td>
<td>Competitive renewal</td>
<td>30-40%, ND</td>
</tr>
<tr>
<td>9. Sr. faculty</td>
<td>Competitive renewal</td>
<td>ND, ND</td>
</tr>
<tr>
<td>10. Sr. faculty</td>
<td>Revised new</td>
<td>40-50%, ND</td>
</tr>
</tbody>
</table>
1: New investigator
Successfully revised application
30-40%, 1-5%

Reviewer comments included:
• Significance: ...key role in host response...highly significant question ✓
• Preliminary studies...polymorphisms in...associated with disease susceptibility... ✓
• Approach: ...major strength...is the depth of the preliminary studies... ✓
• ...hypothesize that...is a critical regulator of...and... ✓
• Aim 1: ...refocused based on study section input... ✓
• Preliminary studies support the feasibility ✓
• ...collaborations...bring strong...support to the project... ✓
• ...a carefully thought out series of experiments will address (a)..., (b)..., or (c).... ✓
1: New investigator
Successfully revised application
30-40%, 1-5%

Aim two...These experiments are novel...

- Dr. ...is aware of the limitations of mouse models of...
- Several alternative strategies are suggested
- Aim 3...innovative experiments...have been designed in response to ...
  ...initial review of this proposal
- Innovation: ...approaches are generally cutting edge
- Overall impact: ...outstanding revised proposal...
- The strengths of the proposal include the focused and novel studies..., the potential of Dr....as a new investigator and the environment...which will clearly augment many of the studies
- Weaknesses are few but include concerns about..., though this deficit can easily be rectified given...
2: Junior faculty
Successfully revised competitive renewal application
12-20%, then 1-5%

Reviewer comments included:
- Approach: ...further improved in several areas ✓
- The applicant has addressed a number of concerns..., and provided additional data ✓
- Aim 2...concern of whether...mice would be viable...addressed by citing that double knockout mice...already exist... ✓
- Aim 3...previous concern in the combined effect of...and...in...has been addressed through inclusion of a separate study of... ✓✗
- Another concern in the production of antibodies...has been mostly alleviated with the availability of... ✓
- Innovation: ...state-of-the-art techniques✓
2: Junior faculty
Successfully revised competitive renewal application
12-20%, then 1-5%

(Continued)

- Investigator(s): ...important discoveries...in top journals...
- Overall impact: ...outstanding application...
- ...multiple, parallel approaches
- ...relevance to...diseases
- ...detailed biochemical characterization of...and...
- ...additional preliminary data...further strengthens the application...
- ...the revision has provided critical details and raised the enthusiasm for this application
3: Junior faculty
Successfully revised new application
10-15%, 10-15%

Reviewer comments included:

• The principal investigator has amassed the expertise and reagents to address a fundamental question in the mechanism of disease regulation.

• There are no significant weaknesses.

• Aims 1 and 2 are important because they will directly link...to...

• These experiments form the bases for understanding how...may function in human disease.

• The proposal is carefully written with a thorough background in... biology and...relevant to the experimental plan.

• Excellent preliminary data provide support for the proposed studies.
4: Senior faculty
Successfully revised application
20-30%; 1-5%

Reviewer comments included:
• Significance: ...hypothesis that...controls...in..., leading to...in the target tissue,...and expression of...symptoms
• ...may explain...aspects that pertain to clinical heterogeneity
• Approach: ...Substantial changes...made to address reviewers concerns
• ...new body of data generated by the investigator
• Aim 1...a number of well-designed experiments
• Aim 2...primary hypothesis of the proposal
• ...analysis of animals before and during clinical onset and genetic tracking will allow identification of...
• ...an improved version
4: Senior faculty
Successfully revised application
20-30%; 1-5%

(Continued)

• ...proposed experiments...demanding, but within the expertise available.

• Aim 3...considered a major weakness...now a well-designed and potentially informative project.

• ... despite...discovery-driven methods, e...hypothesis will guide analysis.

• ...may lead to uneven conditions across experiments and...may fail to faithfully replicate the in-vivo scenario.

• Innovation: ...not entirely novel...focused and hypothesis-driven.

• Investigator(s): ...well-established and respected immunologist...

• Overall impact: ...a rich and demanding array of...experiments.

• ...forthright effort to be responsive to the previous critics.

• Preliminary data are solid and convincing.

• Track record, expertise, and experience are additional strengths.
5: Senior faculty
Successfully revised competitive renewal application
30-40%, then 5-10%

Reviewer comments included:

• This revised application retains its original five specific aims which have been reformulated in order to make them much clearer and focused ✓

• The investigators have been very responsive to the reviewers’ critiques as outlined in the introduction section ✓

• The hypotheses to be addressed are now much more clearly annunciated ✓

• In the 12 months between the initial and revised applications, the investigators have had two additional manuscripts accepted for publication... ✓

• ...innovative projects applying concepts from other diseases to... ✓

• The very innovative projects now have preliminary data ✓
6: New investigator
Unsuccessful application
Not discussed

Reviewer comments included:

- Significance: ...the hypothesis is that...contribute to both...and...  
- Approaches: ...in the...model..., removal of...has no effect on disease course. This result is a bit surprising, considering...
- ...hypothesis is rather vaguely discussed, but previous studies by others have indeed shown that...
- The conclusion...is both...premature and not supported by the data
- Aim 1...Preliminary data...would be helpful...
- The...cell studies seem out of place...
- Aim 3...preliminary characterization studies ...are lacking
- It is also unclear why...is important...
- Recapitulating previous findings...is somewhat unexciting...
- Aim 4...several sub-aims rely on successful outcomes from previous Aims
6: New investigator
Unsuccessful application
Not discussed

(Continued)

- Overall impact: ...strengths...are the expertise..., environment, and ... preliminary data ✓
- ...The overall direction is very broad and frequently descriptive ✗
- ...issues pertaining to the feasibility of these studies, ... ✗
- Resource sharing plan: ...has not been addressed ✗
7: Junior faculty
Unsuccessful new application
30-40%

Reviewer comments included:

• The proposal lacks detailed explanations for some of the technical steps ✗
• References to some of the proposed statistical methods are not included ✗
• Roles of multiple collaborators are not specified. Vague description of modes of collaboration between the multiple researchers involved in the project ✗
• Direct proof was not provided in the form of a publication by the PI that the...strategy will allow detection of... ✗
8: Senior faculty
Unsuccessfully revised application
30-40%, not discussed

Reviewer comments included:

• Significance: ...fine molecular details of...and its involvement in... ✓
• Approach: ...This is based on previous solid...evidence showing... ✓
• Aim 1...not clear...alternative direction... ✗
• Aim 2 ...not clear from ...preliminary data that...it is justified to assume that...is contributing to... ✗
• Some more preliminary data, such as...should be gathered... ✗
• Aim 3...it remains unclear...the relevance of...in the pathogenesis... ✗
• It would be over-simplified if all of the physiological effect of...could be attributed to... ✗
• Overall impact: ...very well written and revised application from an outstanding and experienced investigator... ✓
• ...significance of focusing the whole grant on...is not very apparent ✗
Critique 2:

- Approach: ...these experiments do not get at the molecular mechanism... ✗
- ...fails to incorporate the observation of...reported in the...paper but not discussed in the proposal ✗
- Aim 3 is also largely unchanged...a rather incremental improvement ✗
- Overall impact: ...moderately improved revised application... ✗

Critique 3:

- Overall impact: ...overall hypothesis is clear and well supported by their preliminary data ✓
- ...A major concern...is that the link between...and...has not been well established ✗
- ...proposal to investigate these two pathways...is over-ambitious ✗
- ...approach is too broad ✗
9: Senior faculty
Unsuccessfully revised competitive renewal
Not discussed; not discussed

Reviewer comments included:
• Significance: ...issues of central importance to understanding... ✓
• Approach: ...Because of the late time course of these events, it is hard to understand how these late...events relate to...which was apparent at 40 minutes... ❌
• Aim 1...seem premature for two reasons...we do not know the importance of...in... ❌
• ...a much simpler...can be used... ❌
• The inhibitor studies also could be better planned... ❌
• Innovation: ...not high ❌
• Overall impact: This is a significantly improved application ✓
• ...reliance on primary human samples,...certainly more relevant to human biology,...more limited than what can be done in murine systems ❌
• ...not knowing what the biological importance of...is in... ❌
9: Senior faculty
Unsuccessfully revised competitive renewal
Not discussed; not discussed

(Continued)

Critique 2:

• Approach: ...In response to...the previous review, the investigator has focused on...
  ✔️
  ✖️
• Aim 2...The studies in aim 2 are largely descriptive in nature
  ✖️
• Overall impact: This is a much improved proposal
  ✔️
• ...weaknesses...include the extensive use of...inhibitors without alternative approaches
  ✖️

Critique 3:

• Significance: ...may be relevant to...the normal and disease state
  ✖️
• Overall Evaluation: ...responsive to the previous concerns
  ✔️
• ...but at times lack...cogent discussion of alternatives and priorities
  ✔️
• ...the important...experimental design has to be gleaned from elsewhere in the application
  ✖️
10: Senior faculty
Unsuccessfully revised new application
40-50%, Not discussed

Reviewer comments included:

• Lack of experimental approaches to confirm the proposed hypothesis

• Correlation between...and...could be simply due to..., and the experimental approach lacks...strict control...

• It is well-known that...are involved in...

• The experimental approaches do not carefully consider other etiological factors

• Given the large, interrelated number of...parameters associated with..., it is unclear that the statistical techniques will allow the investigators to meaningfully interpret the association

• The proposal remains largely descriptive and correlative in nature and does not directly provide evidence on the biological basis...
Summary

• Certain failure modes are seen again and again by reviewers

• The scientific or clinical merits of an application may be overshadowed by one or more grantsmanship errors

• While investigators are under pressure to submit grant applications, spending time and resources to preemptively address these concerns may yield better results
In conclusion...

- Please avoid those 6 failure modes in your:
  - Significance
  - Investigator(s)
  - Innovation
  - Approach
  - Environment

- Raise your potential Overall Impact score
- So you won’t even have to see a Summary Statement.
- You’ll just read your Notice of Grant Award, instead!
More Answers

- **Grant Writing**
  - All About Grants Tutorials
  - New Investigator Guide to NIH Funding
  - NIAID Funding Opportunities and Concepts
  - NIAMS Funding Opportunities List
    [http://www.niams.nih.gov/Funding/Funding_Opportunities/filter.asp](http://www.niams.nih.gov/Funding/Funding_Opportunities/filter.asp)
  - How to Write a Human Subjects Application
More Answers

• **Electronic Submission**
  - Electronic Application Resources
  - Finding Help – eRA Commons
  - Finding Help – Grants.gov

• **Grant Review**
  - Center for Scientific Review - Overview of Peer Review Process
    [http://grants.nih.gov/grants/peer_review_process.htm](http://grants.nih.gov/grants/peer_review_process.htm)
More Answers

• **Grant Management**
  - How to Manage Your NIAID Grant Award
    [http://www.niaid.nih.gov/researchfunding/grant/Pages/gm.aspx](http://www.niaid.nih.gov/researchfunding/grant/Pages/gm.aspx)
  - NIAMS Grant Policies & Guidelines

• **Other Topics**
  - Advice on Research Training, Career Awards, and Research Supplements
  - NIH Loan Repayment Programs

• **Example of a Useful University Web Site**
  - UPitt Web Page - Writing and Grantspersonship
    [http://www.oorhs.pitt.edu/Resources/WritingGrantsmanshipResources.aspx](http://www.oorhs.pitt.edu/Resources/WritingGrantsmanshipResources.aspx)
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