

T-R01 Evaluation Report

September 2009

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Executive summary

This report summarizes qualitative and quantitative data gathered through web-based evaluation surveys of the Transformative Research Projects Program (T-R01) applicants and Stage 1/3 reviewers. As part of the NIH Roadmap for Biomedical Research, the primary goal of the T-R01 initiative is to provide support for individual scientists or teams of scientists who propose transformative approaches to important contemporary challenges. For this initiative, transformative projects were required to have the potential to create or overturn existing scientific paradigms through the use of new and novel approaches.

Demographically, the vast majority of the applicants were White and non-Hispanic, male and 40 to 60 years of age. When asked to classify their research, two of the most commonly occurring choices were molecular/cellular/chemical biologists (38% of the applicants) and clinical/translational research (28% of applicants). It is likely the scientific composition of the applicant pool was shaped by the areas of science highlighted in the Request for Applications (RFA) and not representative of the entire scientific community. The majority of applicants thought it unlikely that the concept they proposed for the T-R01 opportunity would receive funding support from other sources. Applicants were asked to evaluate the importance of various proposal sections in communicating their concept's novelty, innovation, and potential for impact. The Challenge and impact section was considered "important" or "very important" by virtually all applicants.

Reviewers were asked to estimate what percentage of the applicants understood the goals of T-R01 program. They responded that at least 50% of the applicants did understand the goals for this important initiative. In contrast, these same reviewers felt a smaller percentage of the applicants were actually capable of conducting transformative research

Background

The goal of the Transformative Research Projects Program (T-R01) is to "support exceptionally innovative, high risk, original, and/or unconventional research with the potential to create new or challenge existing scientific paradigms."¹ In 2009, its first year, the program had funding for up to 60 applications, to the total of \$25 million. Support for the program comes from the NIH common fund.

While the Request for Applications (RFA) states that "projects in any area of NIH interest are encouraged," several areas of "highlighted need" were nevertheless listed. These were as follows:

- Understanding and facilitating behavioral change
- Formulation of novel protein capture reagents
- Functional variation in mitochondria in disease
- Complex 3-Dimensional tissue models
- Transitions from acute to chronic pain

¹ RFA-RM-08-029

- Providing an evidence base for pharmacogenomics.

Applicants were directed to use a specific format, which differed from the traditional R-01 submissions both in length and in content. All applications had to include a 2-page Biosketch; an 8-page Research Plan (with subsections: Challenge and Potential Impact, Approach, Appropriateness of T-R01 Mechanism, Timeline); and a 1-page Bibliography and References.

Each application was reviewed in a three-stage process. In Stage 1, all proposals were screened by a panel of 11 “generalist” reviewers (whose identities were known to the applicants), whose role was to triage about 300 applications per reviewer based on the Challenge/Potential Impact statement. In Stage 2, the applications were evaluated for technical merit by relevant experts. Finally in Stage 3, Stage 1/3 reviewers convened in person to make final decisions based on their own preliminary evaluations and on the input from Stage 2 experts.

Evaluation methodology

CSR administered web-based questionnaires to all T-R01 applicants (720 individuals) and to all Stage 1/3 reviewers (11 individuals). The questionnaires were fielded in February-May of 2009, before the applicants were notified on the status of their application, but after Stage 1/3 reviewers made final decisions. Four hundred and thirty one applicants and seven reviewers responded, resulting in evaluation participation rates of 62% for the applicants and 63% for the reviewers.

The evaluation instruments contained a combination of multiple-choice and open-ended questions. The applicants were asked about their background and funding history; satisfaction with the application process and materials; and characteristics of transformative research. Questions to reviewers included their views on the clarity of instructions; on the review process (in their capacity as Stage 1 and Stage 3 reviewers); and on the applicant pool.

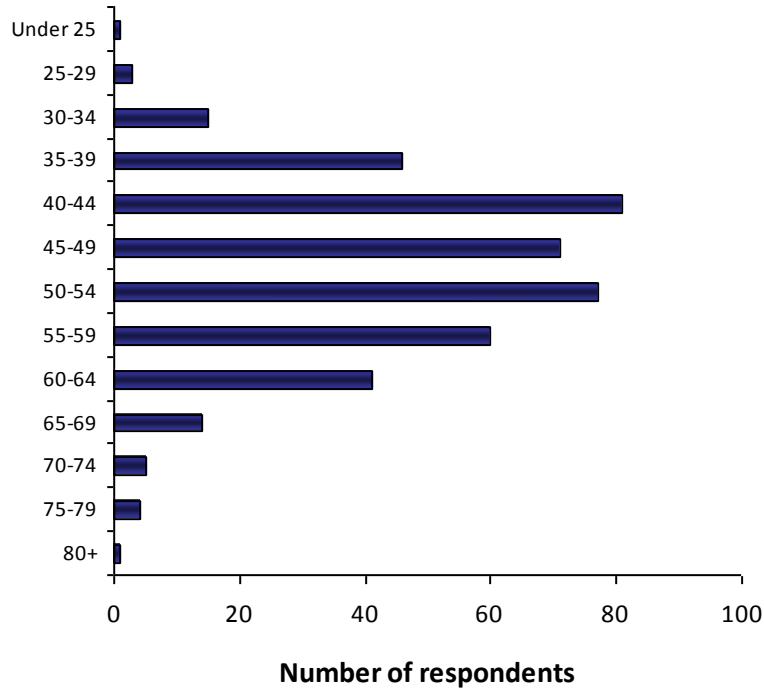
Findings: Applicant Feedback

This section is a summary of the applicants’ answers to multiple-choice and open-ended questions. Questions and answers are not presented in the order they appeared in the questionnaire, but are grouped thematically.

Demographic information

Seven hundred and twenty scientists submitted an application for T-R01 funding. Demographically, the vast majority were White and non-Hispanic (White: 71%; non-Hispanic/Latino: 86%; Asian: 21%; African Americans: 2%; American Indians: <1%). Sixty respondents did not answer the questions on their race/ethnicity. Of these, a few commented that race was irrelevant or “not a biologically valid construct.” Participant age followed a normal distribution, with 67% being 40-60 years old (Figure 1). Curiously, one respondent indicated that he/she was less than 25 years old and another that he/she was over 80 years old (we cannot verify the accuracy of these data).

Figure 1: Applicant Age, N = 431



Scientific focus and funding history

Respondents were asked to classify their research using NIH categories. Two most commonly selected options were molecular/cellular/chemical biologists (38%) and clinical/translational researchers (28%), followed by behavioral/social scientists (10%, Figure 2). Presumably, scientific composition of the applicant pool was shaped by the areas of science highlighted in

Figure 2. Applicant scientific focus, N = 431

Category	N (%)
Molecular, cellular, and/or chemical biology	164 (38%)
Clinical and/or translational research	121 (28%)
Behavioral and/or social sciences	44 (10%)
Physiological and/or integrative systems	39 (9%)
Instrumentation and/or engineering	25 (6%)
Pathogenesis and/or epidemiology	16 (4%)
Quantitative and/or mathematical biology	16 (4%)
No answer	6 (1%)

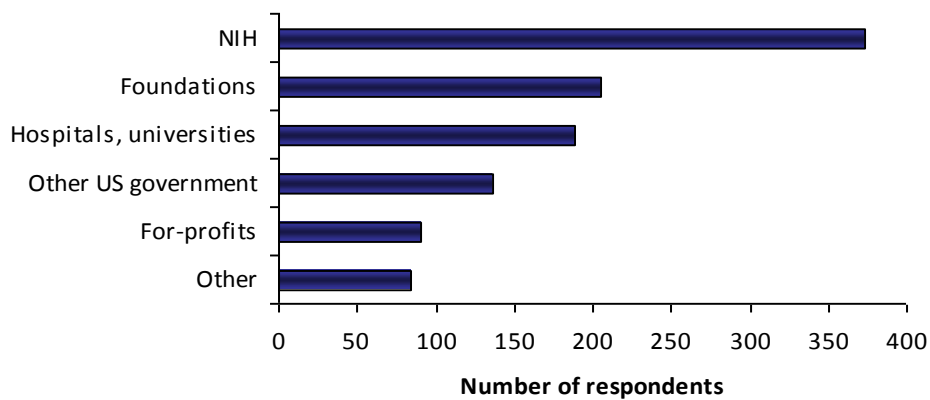
the RFA and is not representative of the entire scientific community. For example, the area “transitions from acute to chronic pain” would attract clinical researchers and “formulation of novel protein capture reagents” would attract chemical biologists. Forty-four respondents indicated additional categories as best describing their research focus. These included

neuroscience, genetics/genomics, imaging, and bioengineering. Several applicants noted that their research was interdisciplinary and spanned more than one category, and one respondent claimed that his/her research fits all categories.

The majority of the applicants intended to use T-R01 funding to explore new scientific ideas: more than 80% claimed that proposed research was a significant departure from their research directions (data not shown). Note that the RFA stated proposed research should represent a completely new direction, which could have biased respondents' answers.

Evaluation findings suggest the program attracted few applicants who have not been previously funded by NIH or have attempted to obtain funding from NIH. When asked to describe their funding history, 382 or 88% reported having applied for an NIH award or grant (data not shown). Furthermore, for many respondents NIH funding represented significant source of the total research support: 65% of the applicants indicated that half or more of their funding comes from NIH, with support from foundations emerging as distant second (Figure 3). For 29 respondents (7%), all of their support comes from NIH (data not shown).

Figure 3: Applicant funding sources, N = 431



Over half of respondents (57%) learned about T-R01 program directly from the NIH, through the

Figure 4. Source of information about T-R01 program, N = 431

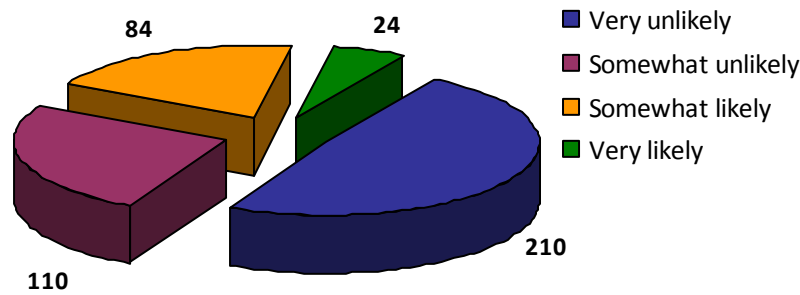
Category	N (%)
NIH guide	147 (35%)
T-R01 or Roadmap website	96 (22%)
Departmental announcement	69 (16%)
Word of mouth	58 (13%)
Do not recall	28 (7%)
Other	31 (7%)

NIH guide or T-R01/Roadmap web site (Figure 4). Additional 29% were notified about the program by their department or heard about it by word of mouth.

The majority of respondents (74%) thought that they were unlikely to receive funding support for their concept from

other sources (Figure 5). The nature of the alternative sources for the remaining 26% has not been explored in the evaluation.

Figure 5: Possibility of receiving funding from other sources, N = 431

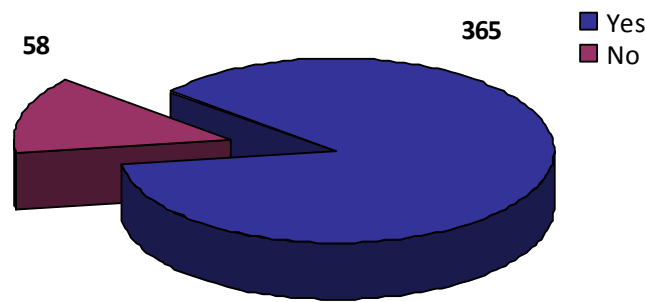


Application process

To provide additional guidance to the applicants, program staff developed a document containing answers to the frequently asked questions (FAQs). When asked whether the RFA and the associated FAQs were helpful in describing the types of projects the program was seeking to fund, 365 (85%) responded in the affirmative (Figure 6).

Respondents who did not find the instructions satisfactory were invited to offer suggestions on how to improve these materials using a text box provided. Three main categories of responses emerged. The most common view was related to the appropriateness of including specific research topics of interest (“highlighted areas”) in the RFA. All comments submitted were negative, describing the topics as “too arbitrary,” “too few,” and “peculiar.” Further, it was unclear to the applicants how directive the areas were meant to be and whether proposals that did not fall within these areas had any chance of being funded. (One applicant recalled thinking that his/her research idea was not within the suggested areas, only to be persuaded to apply by the program staff he contacted.) Some respondents suggested not including any specific areas, others including a wider range of areas. The applicants would have liked for the NIH to be more explicit about what type of research would/would not be funded and what the reviewers would be looking for. One respondent suggested that the RFA should include 1-2 examples of ideas “that would NOT be appropriate, with brief explanation of what aspect would disqualify each.” (Note that this suggestion to “emphasize the distinction from traditional R01” was also made by a Stage 1/3 reviewer).

Figure 6: Number of respondents indicating whether proposal instructions were helpful, N = 431

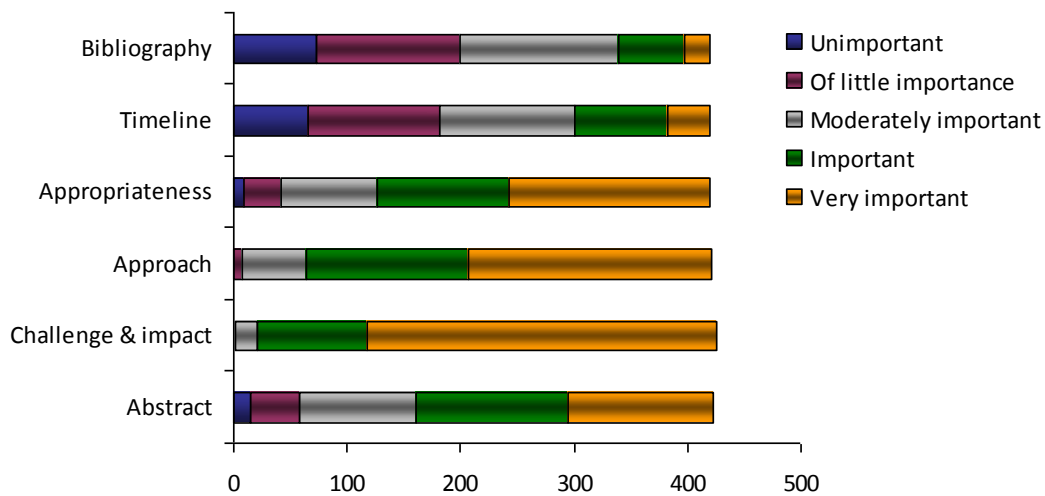


Several respondents were dissatisfied with proposal instructions and/or with the timing of their release. One applicant recalled that the original RFA stated that parts of the proposal should be uploaded as separate items, but that guidance was later changed, “causing confusion and waste of time.” Another respondent noted that NIH released a clarification notice, which redefined the expectations for the proposals, shortly before the application due date, leaving this person with no choice, but to re-write the proposal at the last minute.

A small number of respondents relayed being confused about the length or structure of the proposal. One applicant had trouble understanding what sections were required; another said that he/she could not determine whether the 10 item limit for the biosketch referred to the submitting PI only or to all applying co-investigators (ostensibly, this issue could not be resolved by individuals listed in the RFA as contacts).

The applicants were asked to evaluate the importance of various proposal sections in communicating their concept’s novelty, innovation, and impact. Challenge and impact section was considered “important” or “very important” by virtually all applicants (404 or 94%), followed by approach (357 or 83%), and by the appropriateness of T-R01 mechanism (294 or 68%, Figure 7). Note that these were the same sections consulted by Stage 1/3 reviewers during their initial triage of applications (Figure 12).

Figure 7: Relative importance of proposal sections in communicating research concept, N = 431



Finally, two respondents commented that it was “somewhat unrealistic” to expect that the proposed research would represent completely new direction for the applicant. As one individual put it, “it’s unlikely that people will come up with really superb science and be able to execute it with ideas and experiments on which they have no prelim[inary] data or research credibility.”

While this was not the intent of the question, a number of applicants used the space provided to express concerns about the review of their proposals. One respondent commented being disappointed with the composition of the editorial panel: “they were all from the pharma/gene area and clearly did not have the breadth to review the regenerative proposals that were submitted.” Similarly, another applicant said that “the descriptions of projects did not match the expertise of the review panel.” Yet another applicant noted that there was no indication in the RFA that the review process would be conducted in a way that will “accommodate non-conservative thinking.” Apparently, this respondent had first-hand experience with the NIH study sections, and found it “impossible to believe that T-R01 applications will be reviewed in any way different than regular R01.”

Finally, one respondent appeared to have had trouble with electronic submission. This individual tried to upload two proposals with similar titles (but addressing “different issues and research areas”), but these proposals were perceived by the system as a duplication. The applicant was unable to edit the titles of the documents to fix the problem. Further, because of the submission traffic at this applicant’s institution, part of his/her proposal did not load on the NIH server and was lost. This applicant was later asked by the NIH to submit the missing portion separately and shortly thereafter to withdraw the application (specifics of these events were unclear).

Definition of transformative research

In the questionnaire, the applicants were asked what characterized transformative research and to illustrate their answers with specific examples. Three hundred and fifteen individuals (73%) provided comments (data not shown). The applicants suggested that transformative research should have the following characteristics:

- Takes a discipline into new direction; opens new methodology or new mechanism; generates new technology that will accelerate research within a given field
- Integrates existing technology or ideas; applies existing knowledge to new field; interdisciplinary
- Challenges existing paradigm, hypothesis, or dogma; challenges the status quo
- Closes a knowledge gap
- High risk, high reward; has potential to get into a market place; has potential to affect large number of patients; changes the way healthcare providers treat patients
- New conceptualization of old problem; out-of-the-box thinking
- Addresses significant, important problem
- Asks questions where the answers are not known or obvious; something no one has directly studied; directed at unconventional goals
- “You know it when you see it”
- Is likely to fail; upsets established investigators; not represented in the majority of published papers; contains no preliminary data; lacks precedent
- Validates something that is obvious, yet universally ignored as obvious; connects the dots; elegant
- Will affect the most number of researchers; will dramatically impact science, technology, and society
- Clearly originates from a different perspective
- Can only be known in retrospect

While a small number of respondents referred to their own work as examples of transformative research, most commonly mentioned were famous discoveries of the past 20 years, which had typically led to a Nobel Prize. Two examples most frequently offered were polymerase chain reaction (PCR) and RNAi/micro-RNA. Other examples included nuclear magnetic resonance (NMR), DNA methylation, DNA sequencing, somatic hypermutation of antibody genes, tissue polarity, transdifferentiation, induced stem cells, and controlled gene knock-out in mice.

As was the case with the comments provided in response to the question on improving application materials, many respondents took an opportunity to note that transformative was

not the type of research funded by NIH. One applicant conveyed the skepticism of many, bitterly noting: “you put out a call, we answered, and you still funded the most mundane stuff imaginable.”

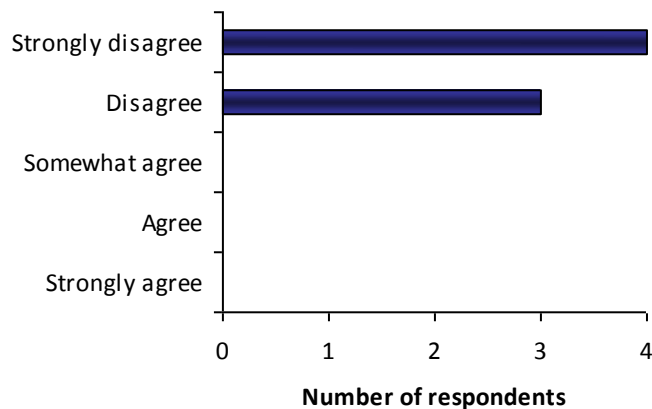
Findings: Reviewer Feedback

This section is a summary of reviewer answers to the evaluation survey. For T-R01 grants, the NIH used an “editorial” review model, whereby all applications are first triaged by 11 generalist reviewers with a subset forwarded to the experts chosen based on the proposal topic. Finally, Stage 1 generalist reviewers meet in person to make final award decisions. The questions explored generalist respondents’ experiences both as Stage 1 and as Stage 3 reviewers (7 of 11 reviewers responded). The summary does not include any data from Stage 2, specialist reviewers.

Proposal instructions

As discussed above, several applicants appeared to be opposed to the concept of including “highlighted areas” of science in the RFA. This view was shared by the reviewers. All reviewers reported that the inclusion of highlighted areas did not facilitate the submission of transformative proposals (data not shown). One reviewer wrote: “I don’t think the inclusion of highlighted areas was particularly helpful. However, it did increase the number of applications that were not competitive and hence the number of applications we had to review.” All reviewers “disagreed” or “strongly disagreed” with the idea of including specific areas of research in future announcements (Figure 8).

Figure 8: Views on the inclusion of highlighted areas of science in the RFA, N = 7

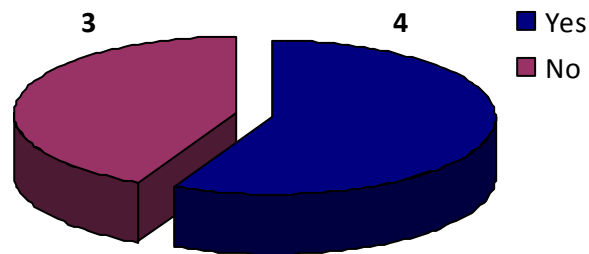


When asked how to change instructions to the applicants to facilitate decisions that must be made during Stage 1 review, reviewers unanimously suggested that the applicants summarize their proposed concept in 100-150 words. Note that it was clear from reviewers' answers that they had discussed how to improve the review process, thus the suggestion to include an abstract represents a collective opinion.

Workload

In the first stage of the review process, 720 applications were divided among 11 generalist reviewers, with about 300 applications assigned per reviewer. Reviewers were asked whether this workload was reasonable. Respondents appeared to be split, with 4 out of 7 answering in the affirmative (Figure 9). Of the 3 reviewers who felt that the workload was excessive, 2 suggested that 200 applications per reviewer would be optimal and 1 that 100 applications would be optimal (data not shown). In our view, reviewer willingness to take on such heavy workload illustrates strong commitment to the idea of high-risk research support.

Figure 9: Reasonableness of reviewer workload, N = 7



Applicant pool

Reviewers were asked to estimate what percentage of the applicants understood the goals of T-R01 program. All reviewers responded that at least 50% of the applicants did so (Figure 10). In contrast, in the opinion of the same reviewers, 25% or fewer of the applicants were *capable* of conducting transformative research (Figure 11).

Figure 10: Number of applicants who understood the goals of the transformative R01 Initiative, N = 7

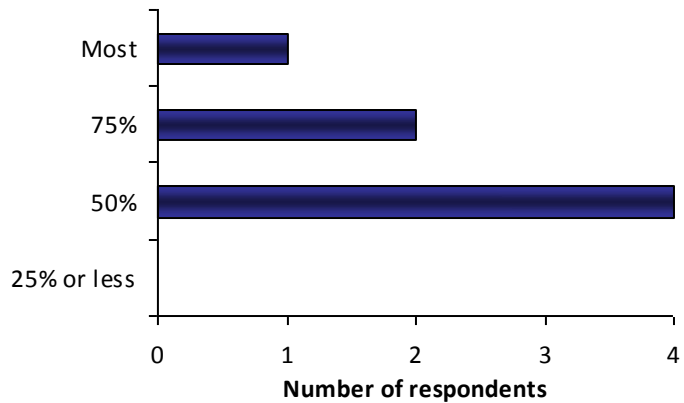
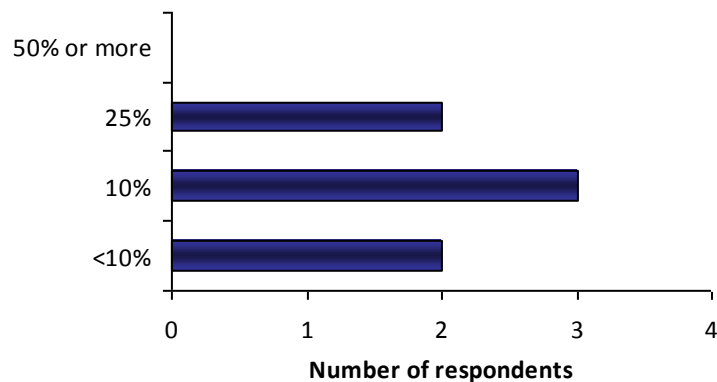


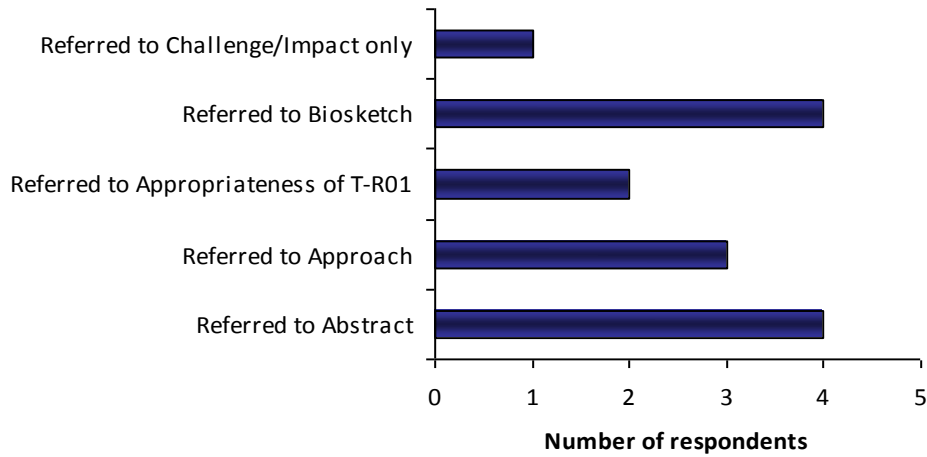
Figure 11: Number of applicants capable of transforming science, N = 7



Review process

While Stage 1 reviewers were asked to focus on a 1-page Challenge and Potential Impact statement to triage the applications, it emerged that all but one consulted other sections (Figure 12). Abstract and biosketch appeared to be most commonly referred to, by 4 out of 6 reviewers. These data suggest that reviewers were not making their decisions based exclusively on the proposed idea, but took into account the applicants' background and credentials. As the total of 13 sections were consulted by 6 reviewers (excluding 1 reviewer who only referred to the Challenge and Potential Impact section), each reviewer referred to 2 other sections, on average, in addition to Challenge and Potential Impact. Again, this thoroughness seems remarkable considering the volume of applications assigned to each Stage 1 reviewer.

Figure 12: Use of proposal sections in evaluating applications by Stage 1 reviewers, N = 7



Several questions examined what influence Stage 2, specialist reviewers had on the peer review outcomes. It emerged from the evaluation that Stage 2 reviewers played a key role in determining which proposals were funded. All generalists asserted that Stage 2 reviewers “often” or “always” had the appropriate expertise to evaluate the technical aspects of the application (Figure 13). Their input was provided in a form that facilitated final decision making (100% of reviewers, data not shown) and was “very helpful” in arriving at a final score (data not shown). Stage 2 comments “sometimes” or “often” dramatically changed the initial assessment of the proposals during Stage 1 review (Figure 14).

Figure 13: Matching of specialist reviewer expertise with technical aspects of the proposal, N = 7

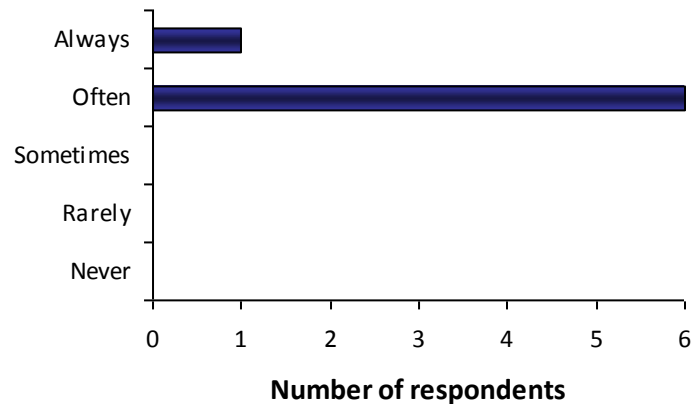
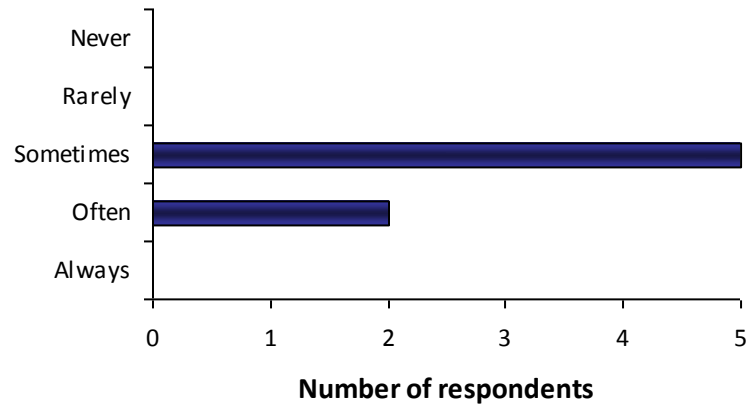


Figure 14: Change in the generalist reviewers' assessments of proposals as a result of Stage 2 input, N = 7



Conclusions

This report is the synthesis of qualitative and quantitative data gathered through web-based census evaluation surveys of T-R01 applicants and Stage 1/3 reviewers. Several important conclusions emerged from the data:

- More than 80% of the applicants claimed that proposed concept was a significant departure from their research directions, although some applicants felt this expectation was unrealistic
- T-R01 attracted few applicants who were new to NIH; 65% of the applicants receive at least half of their research support from NIH
- FAQs developed by the program were helpful to most respondents (85%)
- Both applicants and reviewers appeared to be opposed to the idea of “highlighted areas;” reviewers claimed that including highlighted research areas increased the number of non-competitive applications and reviewer workload
- The applicants were unclear whether proposals on topics that were outside of highlighted areas would be funded
- Some applicants were confused about the length and structure of the proposal and a few were dissatisfied with the late timing of release of RFA-associated documents
- Many applicants were skeptical that the review process would result in the funding of transformative proposals; some noted a mismatch between Stage 1 reviewer expertise and highlighted areas
- Reviewers suggested including short summary of proposed concept in the application
- Four of seven reviewers felt that their workload was appropriate, the rest suggested reducing the number of applications per reviewer to 100-200
- Reviewers said that more than 50% of the applicants understood the requirements of the RFA, but less than 25% were capable of transformative research

- Six of seven reviewers referred to sections other than Challenge/Potential Impact in the initial stage of the review
- Stage 2 reviewers played key role in the review process: all Stage 1/3 reviewers relied on Stage 2 reviewer input in arriving at the final score.