U.S. Department of Health & Human Services

NIH Center for Scientific Review

CSR Advisory Council Workgroup: Simplifying Review Criteria for Clinical Trials

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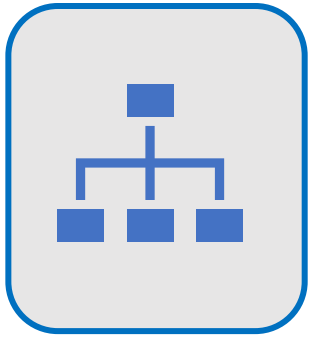
Recommendation 1:
Reorganize review criteria to focus on key questions.



- Reorganize the five core review criteria into three factors, “Importance of the Science”, “Feasibility and Rigor”, and “Investigator(s) and Environment”.

- Intention is to focus reviewers’ attention on the big picture questions that should drive scores
  - *Should it be done*? → Importance of the science
  - *Can it be done well?* → Feasibility and rigor
  - *Will it be done?* → Investigators and environment

- Applications to receive three factor scores plus an Overall Impact score.

Applications would receive Overall Impact plus 3 factor scores

I. Importance of the Science (scored)

a. ***Significance (not scored):*** Evaluate the scientific value of the knowledge likely to be gained

b. ***Innovation (not scored):*** Evaluate the novelty and creativity of the ideas

"Work that is not highly significant must not be rated highly important."

II. Feasibility and Rigor (scored)

a. Approach (not scored): technical competence, rigor, and feasibility of design, methods, models, analysis

b. Innovation (not scored): Evaluate the novelty and creativity of approach

"Projects need not be strong on both to justify a strong score."

III. Investigators and environment (scored)

a. Investigators (not scored): evaluate…with respect to the likelihood that the project will be accomplished and will produce important new knowledge

b. b. Environment (not scored): how will the environment contribute to successful execution of the proposed project.

"Evaluate the likelihood that the proposed project will be executed well, that the project will be productive and rigorous, and that scientifically valuable outcomes will result"

Additional Recommendations:

#2. Define each criterion and factor conceptually

- Definitions, not questions.

#3. Alter templates to focus reviewer attention on score driving factors.

- Replace “Strengths” and “Weaknesses” below each scored criterion with “Major Score-Driving Factors” and “(optional) “minor points”

#4. Clarify reviewer responsibility for evaluating the budget

- 3 response options (appropriate, excessive, inadequate)

#5. Relieve reviewers of responsibility for most “additional review considerations”.

- Biohazards, resource sharing plans, authentication plans, etc. should be reviewed by NIH program staff

Recommendation 6:
Convene an additional workgroup for review criteria for clinical trials applications.

- Retain the goals of reducing reviewer burden and producing better review outcomes. Work with the proposed framework.

- Recognizing that there are unique considerations for clinical trials, additional input from scientists with this specific focus and expertise is needed.

- We sought investigators with expertise in different types of clinical trials

Simplifying Review Criteria Workgroup Members

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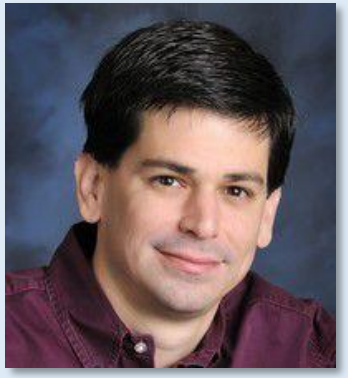

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How are CT applications different?

- Different FOAs
- Registration is required
- HS and CT Information form
  1. title & registration
  2. study focus, inclusions
  3. protections, monitoring
  4. study design: detailed description, outcome measures, statistical power
- Review criteria are modified
  - ❑Standard 5 criteria have expanded definitions
  - ❑6th Criterion “Timeline” is required

Why are CT applications different?

- Driven by widespread concern about frequent failures to replicate preclinical work in clinical trials and a GAO that report highlighted difficulties that NIH had in tracking/reporting clinical trials outcomes.
- Many clinical trials failed to report any outcome at all
- Not based in changes in statute/regulation.

- NIH CT policy changes reflect efforts to improve rigor, reproducibility, tracking, reporting

Charge to committee

- Recommend how clinical trial review criteria should be modified to reduce reviewer burden and improve review outcomes.
- Start with the recommendations of the non-CT RPG group.
- Consider the full range of clinical trials, BESH, mechanistic clinical trials, and interventional trials
- Remember the problems that led to different CT criteria

First meeting, major points

- The three-factor structure proposed by the initial workgroup can be translated well to the review of clinical trials-- with modifications, especially for the Feasibility and Rigor factor

- The additional material required in the HS/CT information forms is burdensome to both applicants and reviewers and does not drive review outcomes.

First meeting, ideas to work with

- Alternatives for reducing applicant and reviewer burden:
  - assign reviewers different roles when reviewing applications (administrative review vs. experimental design review)
  - have some elements reviewed (or further developed) by program on the small number of applications that go forward to likely funding.

- "Timeline" not a useful criterion at peer-review level. Better evaluated/developed by program, along with milestones

- Current "additional" CT criteria are largely duplicative of standard criteria.

- Dx/Tx trials have features other science does not
  - Critical role of feasibility
  - Reliance on prespecified, fixed methods that require great detail to adequately evaluate

Next

- ❑ Members are writing proposed modifications to the 3-factor framework from the (March) interim report
- ❑ The compilation of those ideas will be the basis for continuing work
- ❑ BESH, mechanistic, and “traditional” dx/tx phased trials are very different and may not be amenable to a single approach.

Discussion