U.S. Department of Health & Human Services

NIH Center for Scientific Review

Managing Reviewer Burden

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Presentation Outline

- What do we mean by “reviewer burden”
- Sources of reviewer burden
- Managing burden: Case studies of NIH’s clinical trial policy
  - IPTA (SRO: Dr. Miriam Mintzer)
  - AUD (SRO: Dr. Ying-Yee Kong)

Focus: Burden related to NIH review policies

Affect Score

Scored Review Criteria (+ Clinical Trials)

Significance (Premise)

Investigators (+Multiple PIs)

Innovation

Approach (Rigor, SABV)

Environment

Additional Review criteria

Study timeline (for CTs)

Human Subjects (+ DSMP for CTs)

Inclusion of Women, Minorities, Children (HS)

Vertebrate Animals

Biohazards

Resubmission/Renewal/Revision

Additional Review Considerations

Foreign Organization

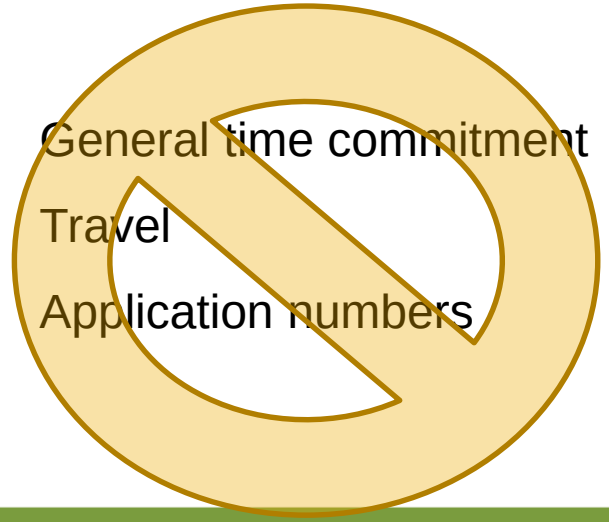
Select Agents

Resource sharing (Data, Model Organisms, GWAS/Genomic)

Authentication

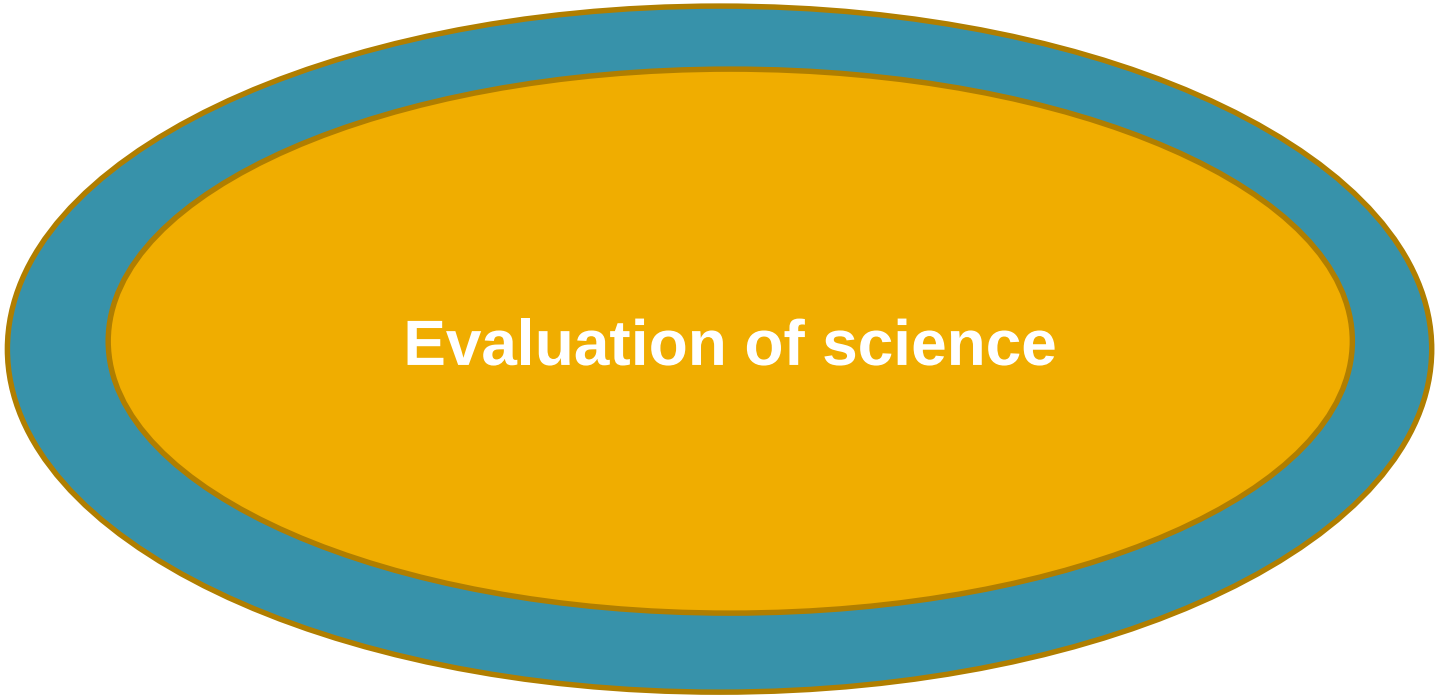
Budget/Period of support

Don't Affect Score



Why Burden Matters

- Availability and participation of reviewers
- Determining appropriate workloads
- ➢ Maintaining focus on evaluation of science/potential impact



Where is reviewer burden coming from?
What is contributing to reviewer burden?

Volume: Information overload

- All together, over 300 pages of instructions
- https://grants.nih.gov/grants/peer/reviewer_guidelines.htm

Consolidated List of Reviewer Documents

Note: *Click here for critique templates, mechanism specific review guidelines and criteria*

Conflict of Interest Information

- Pre-and-Post-Meeting COI Certification Changes in IAR PDF – 26 KB (08/13/2018) NEW
- NIH Conflict of Interest Rules PDF – 33 KB (03/18/2015)
- NIH Pre-review Certification PDF – 36 KB (09/20/2011)
- NIH Post-review Certification PDF – 22 KB (09/20/2011)
- Conflict of Interest Guidance: Contract Reviews PDF – 37 KB (03/16/2015)
- Conflict of Interest Guidance: Grant Reviews PDF – 36 KB (03/16/2015)
- Protecting the Security of NIH Grant Applications PDF – 48 KB (08/19/2013)

Review Criteria Information

- Reviewer Guidance_Clinical Trial Applications 2018 PDF - 185 KB (02/21/2018) NEW
- sIRB guidance summary Peer Reviewers PDF - 266 KB (02/21/2018) NEW
- Applications Proposing Use of Human Embryonic Stem Cells PDF – 123 KB (03/21/2016)
- Budget and Period of Support Information PDF – 284 KB (03/05/2012)
- Frequently Asked Questions for Reviewers on NIH Application Submission PDF – 32 KB (03/18/2015)
- Guidelines for the Review of the Human Subjects Section PDF – 272 KB (02/21/2018) NEW
- Guidelines for the Review of Inclusion PDF – 153 KB (04/05/2016)
- Overall Impact vs Significance PDF – 138 KB (03/21/2016)
- Resource Sharing Plans PDF – 73 KB (03/18/2015)
- Review Criteria at a Glance – Master PDF – 90 KB (03/09/2018) NEW
- Review Criteria at a Glance – Research PDF – 50 KB (03/09/2018) NEW
- Review Criteria at a Glance – Training PDF – 39 KB (03/09/2018) NEW
- Review Criteria at a Glance – Other PDF – 34 KB (03/09/2018) NEW
- Reviewer Guidance on Rigor and Transparency PDF – 158 KB (11/18/2016)
- Reviewer Guidance to Evaluate Sex as a Biological Variable (SABV) PDF – 232 KB (08/8/2016)
- Revision Applications PDF – 87 KB (12/18/2015)
- Worksheet for the Vertebrate Animals Section (VAS) PDF – 161 KB (06/22/2017)

Orientation Information

- Ban on Lobbyists Serving on Advisory Committees PDF – 21 KB (03/18/2015)
- Chair Orientation PDF – 120 KB (07/26/2018) NEW
- NIH Confidentiality and Nondisclosure Rules PDF – 16 KB (07/16/2015)
- Registration Instructions for NIH reviewers to Receive Reimbursement and Honoraria PDF – 367 KB (07/01/2014)
- NIH Reviewer Orientation PDF – 220 KB (11/18/2016)
- NonFederal Peer Review Travel Guidelines PDF – 225 KB (09/01/2014)
- Working with the Review Critique Templates PDF – 202 KB (12/18/2015)

Scoring Information

- Additional Scoring Guidance for Research Applications PDF – 174 KB (03/05/2013)
- Additional Scoring Guidance: Applications for Fellowships, Career Awards, and Institutional Training Grants PDF – 574 KB (05/15/2013)
- Scoring System and Procedure PDF – 70 KB (03/18/2015)

Increasing complexity

Multiple sets of review criteria

Approach

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

If the project involves human subjects and/or NIH-defined clinical research, are the plans to address 1) the protection of human subjects from research risks, and 2) inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion or exclusion of children, justified in terms of the scientific goals and research strategy proposed?

In addition, for applications proposing clinical trials:

Does the application adequately address the following, if applicable:

Study Design

Is the study design justified and appropriate to address primary and secondary outcome variable(s)/endpoints that will be clear, informative and relevant to the hypothesis being tested? Is the scientific rationale/premise of the study based on previously well-designed preclinical and/or clinical research? Given the methods used to assign participants and deliver interventions, is the study design adequately powered to answer the research question(s), test the proposed hypothesis/hypotheses, and provide interpretable results? Is the trial appropriately designed to conduct the research efficiently? Are the study populations (size, gender, age, demographic group), proposed intervention arms/dose, and duration of the trial, appropriate and well justified?

Are potential ethical issues adequately addressed? Is the process for obtaining informed consent or assent appropriate? Is the eligible population available? Are the plans for recruitment outreach, enrollment, retention, handling dropouts, missed visits, and losses to follow-up appropriate to ensure robust data collection? Are the planned recruitment timelines feasible and is the plan to monitor accrual adequate? Has the need for randomization (or not), masking (if appropriate), controls, and inclusion/exclusion criteria been addressed? Are differences addressed, if applicable, in the intervention effect due to sex/gender and race/ethnicity?

Are the plans to standardize, assure quality of, and monitor adherence to, the trial protocol and data collection or distribution guidelines appropriate? Is there a plan to obtain required study agent(s)? Does the application propose to use existing available resources, as applicable?

Data Management and Statistical Analysis

Are planned analyses and statistical approach appropriate for the proposed study design and methods used to assign participants and deliver interventions? Are the procedures for data management and quality control of data adequate at clinical site(s) or at center laboratories, as applicable? Have the methods for standardization of procedures for data management to assess the effect of the intervention and quality control been addressed? Is there a plan to complete data analysis within the proposed period of the award?

Involve complex concepts, specific definitions, and exceptions

Checklist for Applicants and Reviewers: Vertebrate Animals

Performance Site

☐	If the applicant's institution is not where animal work will be performed, are all collaborative performance sites identified?
☐	If more than one performance site is planned, are descriptions of animal use addressing the required criteria provided for each site?

1. Description of Procedures (Vertebrate Animals Section)

Are the following addressed for all species?

☐	Species
☐	Strains
☐	Ages
☐	Sex
☐	Total number of animals by species
☐	Concise description of proposed procedures on live animals (i.e., sufficient information for evaluation)
☐	Source, only if dogs or cats are proposed

2. Justifications (Vertebrate Animals Section)

Are justifications provided?

☐	Choice of species is appropriate for proposed research
☐	Why research goals cannot be accomplished using an alternative model (e.g., computational, human, invertebrate, *in vitro*)

3. Minimization of Pain and Distress (Vertebrate Animals Section)

Are interventions to minimize discomfort, distress, pain, and injury described? (Examples below)

☐	Circumstances relevant to the proposed work, when animals may experience discomfort, distress, pain, or injury
☐	Procedures to alleviate discomfort, distress, pain, or injury
☐	Identify (by name or class) any tranquilizers, analgesics, anesthetics, and other treatments (e.g., antibiotics) and describe their use
☐	Provisions for palliative care or housing that may be necessary after experimental procedures
☐	Plans for post-surgical care, if survival surgeries are proposed
☐	Indicators for humane experimental endpoints, if relevant

4. Method of Euthanasia (Cover Page Supplement / PHS Fellowship Supplemental Form)

☐	If answer is "No" to the question "Is method consistent with AVMA guidelines?", is the method described and a scientific justification provided?

Pace of change

- 2009 **Enhancing Peer Review**
- 2010
- 2011
- 2012 Budget clarification
- 2013 **Scoring table**
- 2014
- 2015 Resource sharing
- **2016** Human stem cells, Inclusions, **Rigor/Transparency, SABV**
- 2017 Vertebrate animals
- **2018** **Clinical Trials,** sIRB, Human subjects
- **2019** **Inclusion across the life span, updates to Rigor/Transparency**, HS exemptions

Policies announced before they affect review

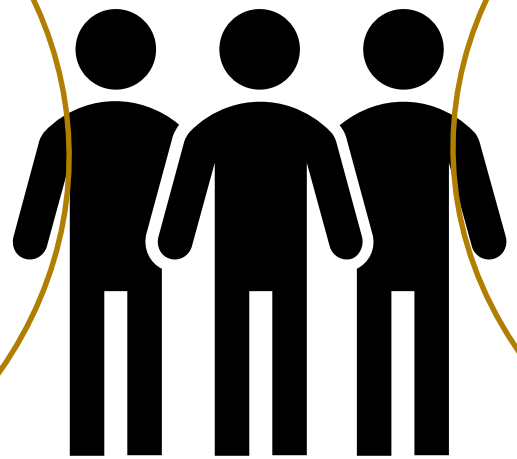
- Example: NOT-OD-18-228 : NIH & AHRQ Announce Upcoming Updates to Application Instructions and Review Criteria for Research Grant Applications
  - replacing “scientific premise” with “rigor of the prior research”…
  - inclusion of individuals of all ages (including children and older adults)…
  - number of human subjects exceptions categories

- Confusion between what’s coming and what’s relevant now.

Policy information/guidance that differs across roles

- Reviewers are also PIs.

Dear applicants,
"Correctly identifying whether a study is considered by NIH to be a clinical trial is crucial to how you will:
- Select the right NIH FOA…
- Write the research strategy and human subjects sections…
- Comply with appropriate policies and regulations…"



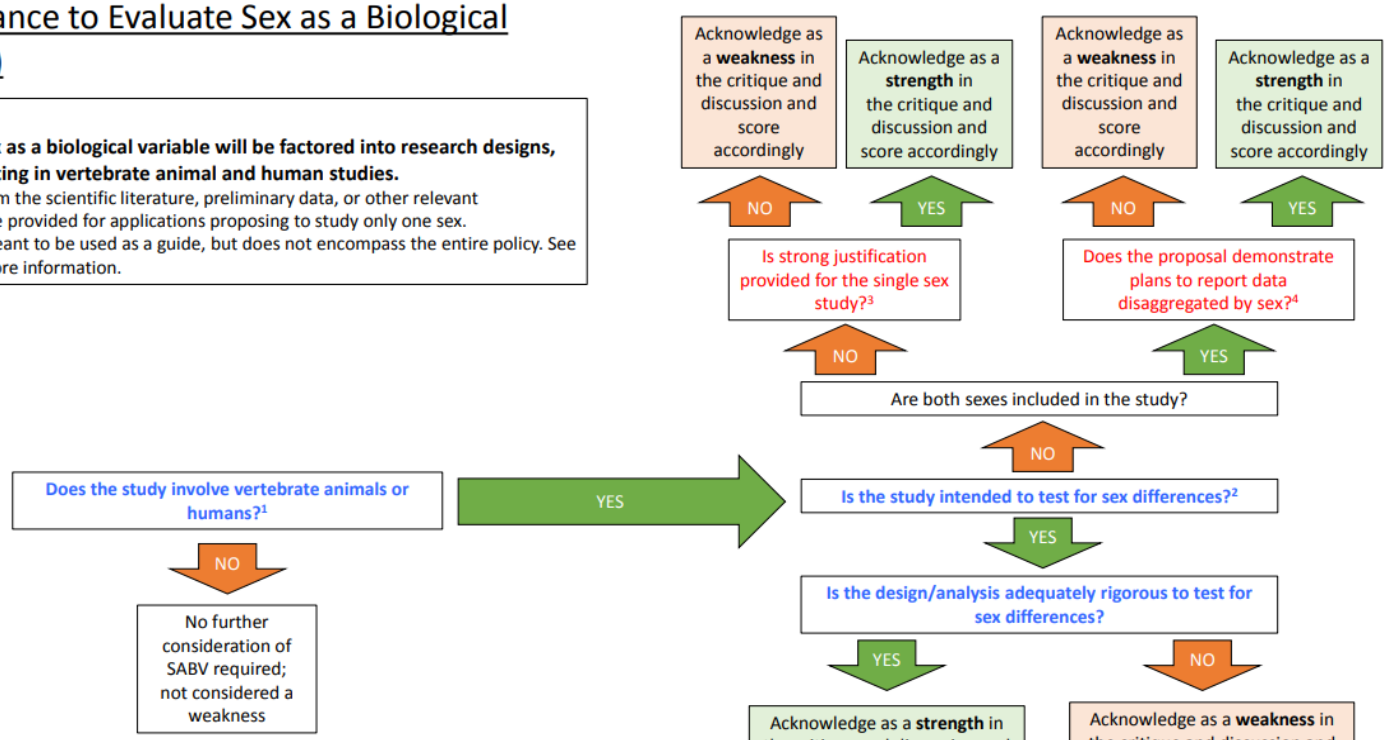
Dear reviewers,
"…We are asking reviewers to review applications submitted for the January 25, 2018 due date and beyond based on the clinical trial designation from the electronic cover page of the application, using the matching review criteria from the FOA. There will be **no discussion in the meeting of whether that designation is correct or not."**

Policy application differs across science

Reviewer Guidance to Evaluate Sex as a Biological Variable (SABV)

Main points

- **NIH expects that sex as a biological variable will be factored into research designs, analyses, and reporting in vertebrate animal and human studies.**
- Strong justification from the scientific literature, preliminary data, or other relevant considerations must be provided for applications proposing to study only one sex.
- This decision tree is meant to be used as a guide, but does not encompass the entire policy. See NOT-OD-15-102 for more information.



Notes

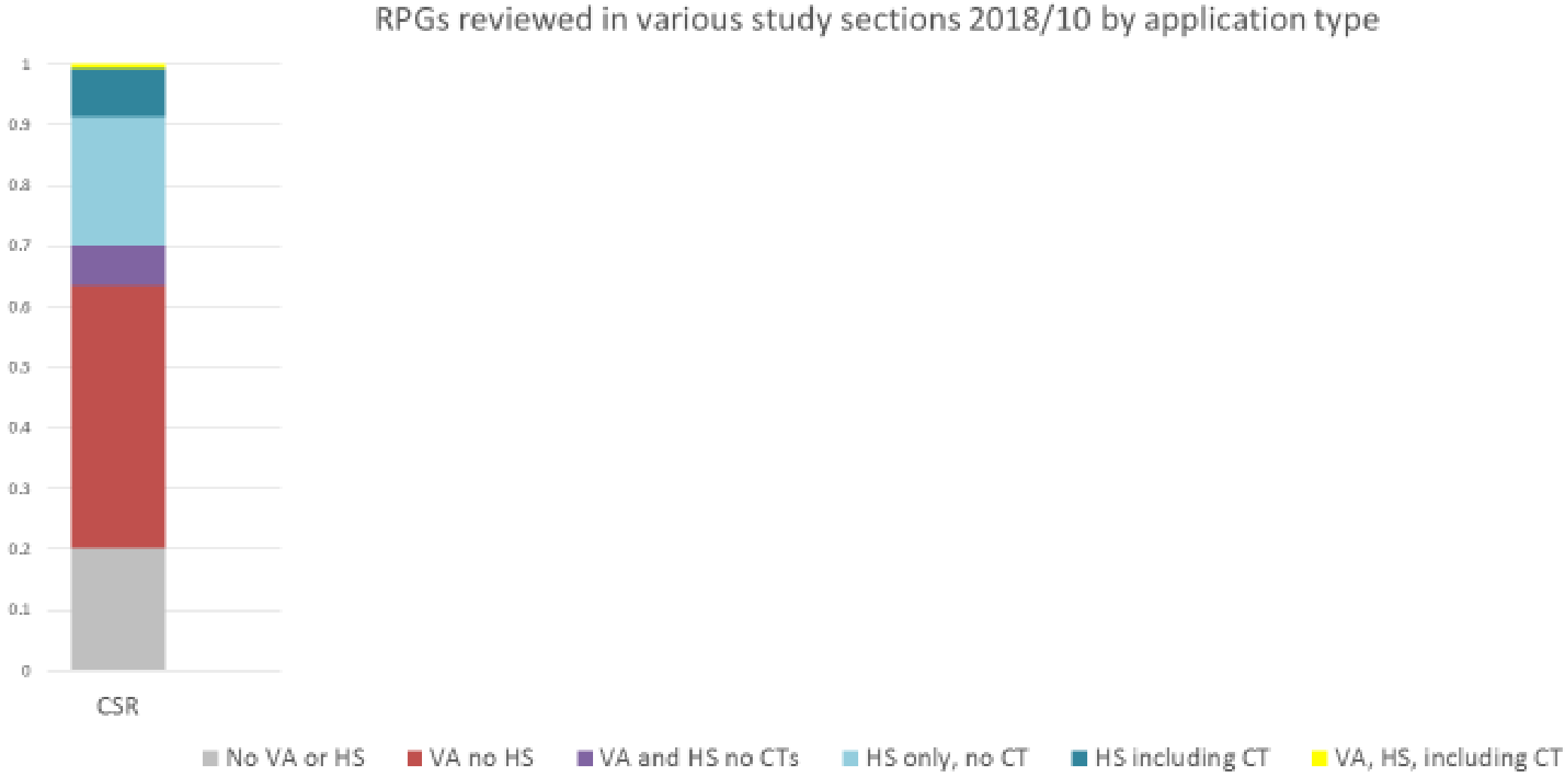
[1] See FAQs on inclusion, primary cells and tissues, and established cell lines.

[2] See FAQs on considering sex as a biological variable and use of males and females in basic research.

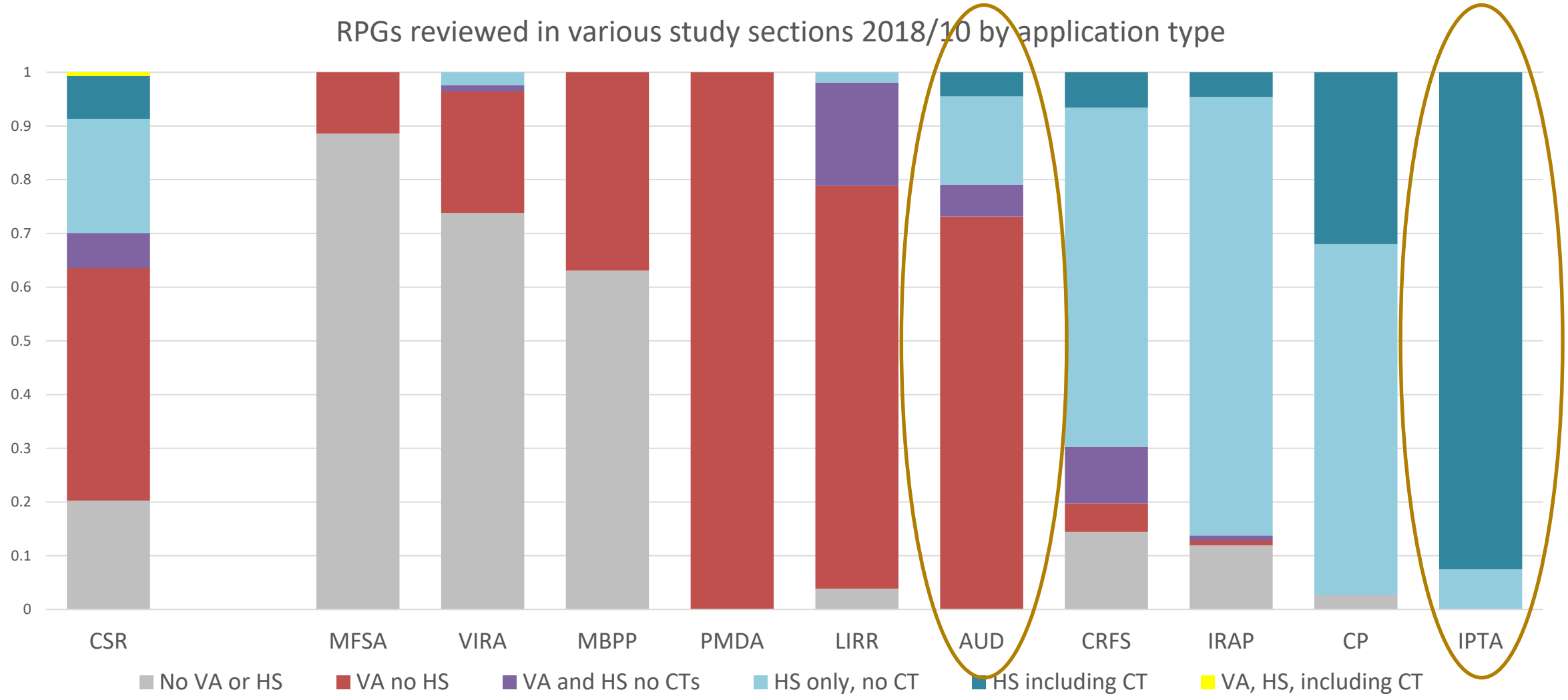
[3] See FAQ on justification of single sex studies.

[4] Based on the research question and availability of relevant data, statistically powered comparisons between the sexes may not be required. Analyzing and publishing sex-based data, even in the absence of powered sex differences analyses, would permit the consideration of the influence of sex in the interpretation of study results and the appropriate generalization of research findings.

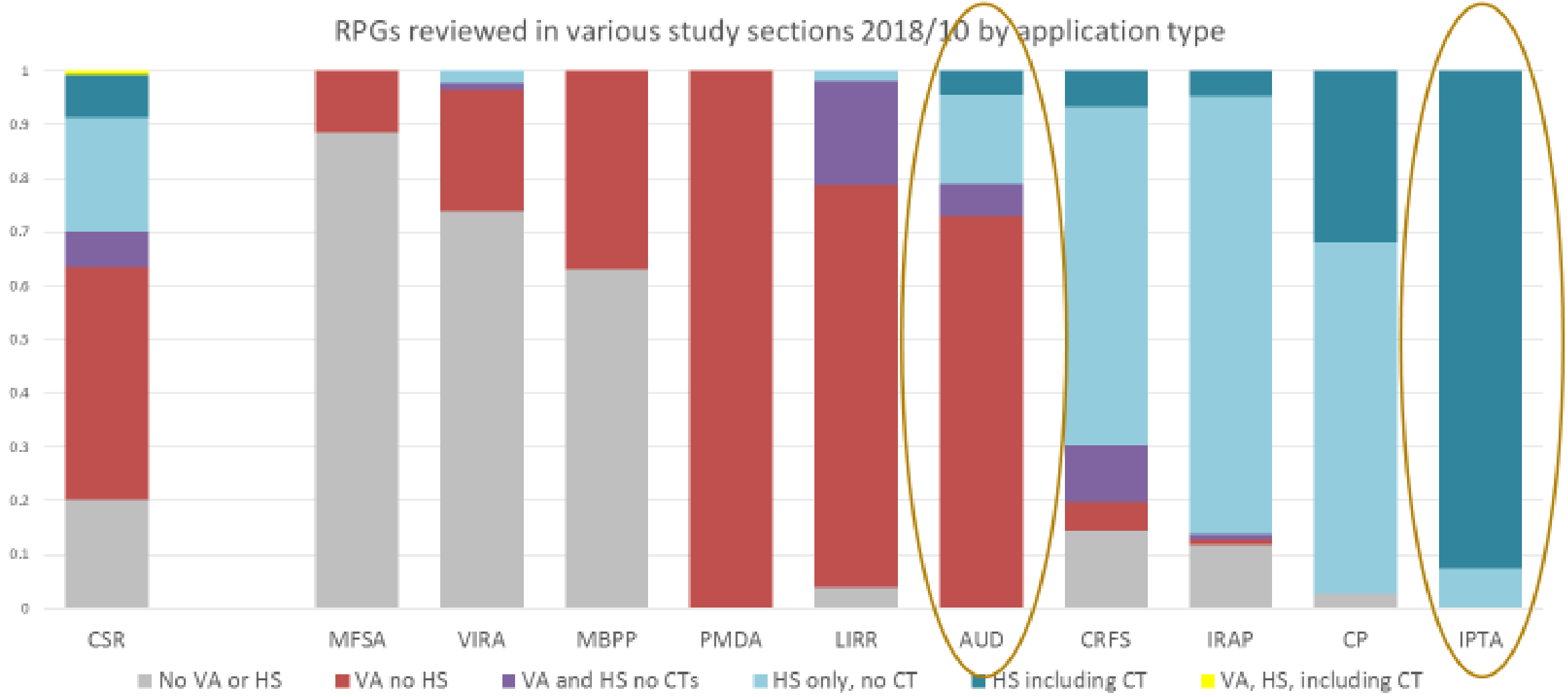
Different policies relevant across applications



Different policies relevant across applications



Different policies relevant across applications



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Managing reviewer burden in clinical trial applications
Case study 1

Miriam Mintzer, Ph.D.
Interventions to Prevent and Treat Addictions (IPTA) study section

Interventions to Prevent and Treat Addictions (IPTA)

- Scope: Clinical applications testing interventions to prevent the onset of addictive and related problem behaviors, prevent the progression of substance use to abuse, curtail the progression of substance abuse to dependence, prevent relapse, and treat substance use disorders and other addictive behaviors.

- ~ 70-90 applications reviewed per round

- ~ 95% of applications meet definition of Clinical Trial (CT)

- 100% of standing members (15 PhD/5 MD) conduct CTs

Nature of Reviewer Burden

- Longer applications for CTs (additional section w/o page limit)
- Key information dispersed across multiple sections
- Redundant (and sometimes conflicting) information across sections
- Expanded review criteria for CTs (additional considerations within each core criterion; new Study Timeline criterion)
- Limited reviewer time

Strategies to Minimize Burden

- Assign fewer applications per reviewer
- Present CT policies and expanded review criteria as extension of Rigor and Transparency initiative
- Emphasize big picture (what's relevant to this specific project?)
- Focus training on scientific (vs. administrative) aspects
- Provide feedback on critique drafts
- Keep communication clear and concise
- Respect reviewers' time throughout review process

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Case study 2

Ying-Yee Kong, Ph.D.
Auditory System (AUD) study section

Auditory System (AUD)

- Scope: Applications studying the structure and function of the auditory and peripheral vestibular systems in human and animal models. Research emphasizes mechanisms underlying normal and abnormal function in the auditory and vestibular systems, and/or ways to improve diagnosis and treatment of auditory and vestibular diseases.
- ~ 65-80 applications reviewed per round
- ~ 5% of applications were identified as Clinical Trials (CT) by the applicants in the 2018/10 and 2019/01 Council rounds
- 25% of standing members conduct CTs

Nature of Reviewer Burden

- Longer applications for CTs (additional section with no page limit) with key and somewhat redundant information dispersed across multiple sections
- Confusion over broadened CT definition to include different types of CTs (mechanistic vs. interventional)
- Many have little experience with human subject studies – difficult to effectively evaluate CT applications (additional considerations within each core criterion; new Study Timeline criterion)

Strategies to Minimize Burden

- Alert reviewers assigned to the CT applications and provide additional training
- Emphasize big picture perspective (Overall Impact, Significance), while highlighting how the expanded review criteria (e.g., study timeline, statistical analysis) are in line with previously established rigor and transparency policies
- Recruit additional experts to the panel when needed
- Offer opportunities to review and provide feedback on drafts of written critiques before submission deadlines

CSR Advisory Council Input