NIH Collaboratory

Health Care Systems Research Collaboratory

Rethinking Clinical Trials®

Topic 10: Developing a Compelling Application

Marcel Salive, MD, MPH, National Institute on Aging

Collaboratory ePCT Training Workshop

Outline

- Which Institute?
- Which FOA?
- Strategies for success
- Resources
- Q&A

Understand NIH: find the right fit

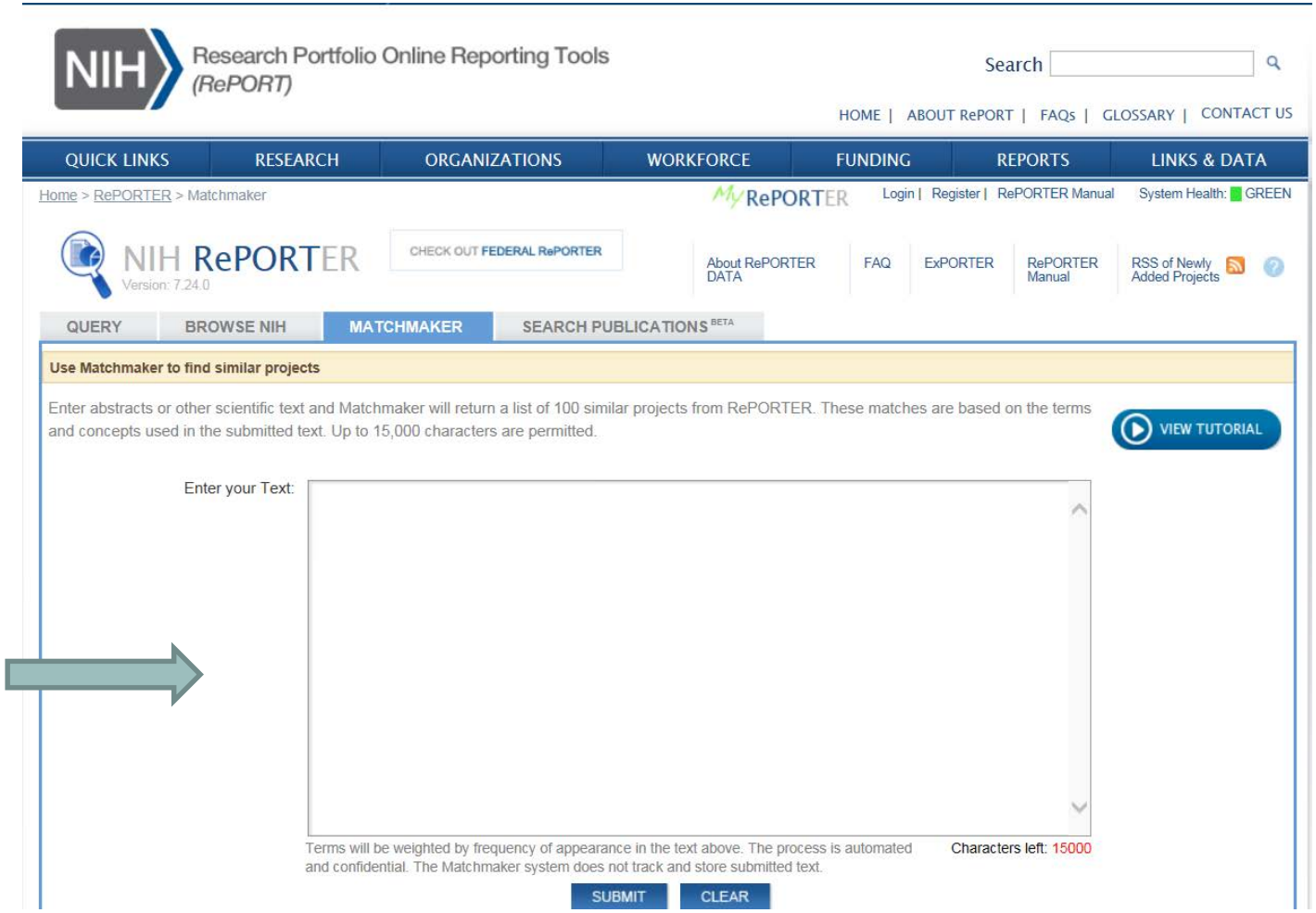
Where's the money?

- NIH is made up of 27 institutes and centers ICs award >80% of the NIH budget each year
- Each IC has a budget and a director, and typically their own review for large trials

IC mission and priorities

- Focus on a specific disease area, organ system, or stage of life
- Check their website
- Use Matchmaker tool in NIH RePORTER for suggestions
- Speak with program officials
- Consult your mentor & colleagues

NIH RePORTER



Source: https://projectreporter.nih.gov/reporter_matchmaker.cfm

Matchmaker results

Grant vs cooperative agreement

Under assistance relationships:

- Grants (R) are used when no substantial programmatic involvement is anticipated between the Federal agency and the recipient during performance of the assisted activity
- Cooperative agreements (U) are used when substantial programmatic involvement is anticipated between the Federal agency and the recipient during performance of the assisted activity

- Not necessarily important for developing the application

Source: P.L. 95-224, NIH Manual 4815

NIH Research Collaboratory: RFA-RM-16-019

Scientific contacts from participating NIH Institutes and Centers

NCCIH	Robin Boineau	**NIDA**	Sarah Duffy
NCI	Erica Breslau	**NIDCR**	Dena Fischer
NHLBI	Barbara Wells	**NIDDK**	Andy Narva
NIA	Marcel Salive	**NIMH**	Jane Pearson
NIAAA	Brett Hagman	**NINDS**	Robin Conwit
NIAID	Clayton Huntley	**NINR**	Jeri Miller
NIAMS	Chuck Washabaugh	**ODP**	Rachael Ballard
NICHD	Sue Marden		

Which study section?

- Mostly Institute-specific special emphasis panels
- CSR Study sections
  - **Health Services Organization and Delivery Study Section**
  - Health services research studies that include multidisciplinary investigations of the organization, delivery, utilization, and outcomes of health services, including availability, access and acceptability; quality of care; costs and cost-effectiveness; *comparative effectiveness*; and financing of health care. Clinical study settings include inpatient, outpatient, sub-acute, acute, community-based, rehabilitative, and long-term care.
- An important question to discuss with NIH program staff, particularly with respect to pragmatic vs explanatory trial

Source: https://public.csr.nih.gov/StudySections/IntegratedReviewGroups/HDMIRG/HSOD/Pages/default.aspx

2017 NIH RFAs: RM-16-019 AG-17-059

- Demonstration Projects that include an efficient, large-scale pragmatic clinical trial; Alzheimer focus
- Multiple NIH Institutes, topics vs NIA
- Collaborate with 2+ HCS, n/a
- Part of NIH Collaboratory vs standalone
- Mechanism UG2/UH3 vs R21/R33

Review Criteria RFA-RM-16-019

Scored Criteria

- Significance
- Investigators
- Innovation
- Approach
- Environment

Additional Review Criteria

- **Milestones**
- Resources and Data Sharing Plan
- **Software Sharing Plan**
- Protection of HS
- Inclusion of Women, Minorities & Children
- Biohazards

All these aspects are considered by reviewers and they do influence the "Overall Impact" score of an application

Several review criteria, as well as the language under the criteria in this FOA, are NOT STANDARD; they are specific for this FOA – READ CAREFULLY

Pragmatic trials of managing multimorbidity in Alzheimer's disease

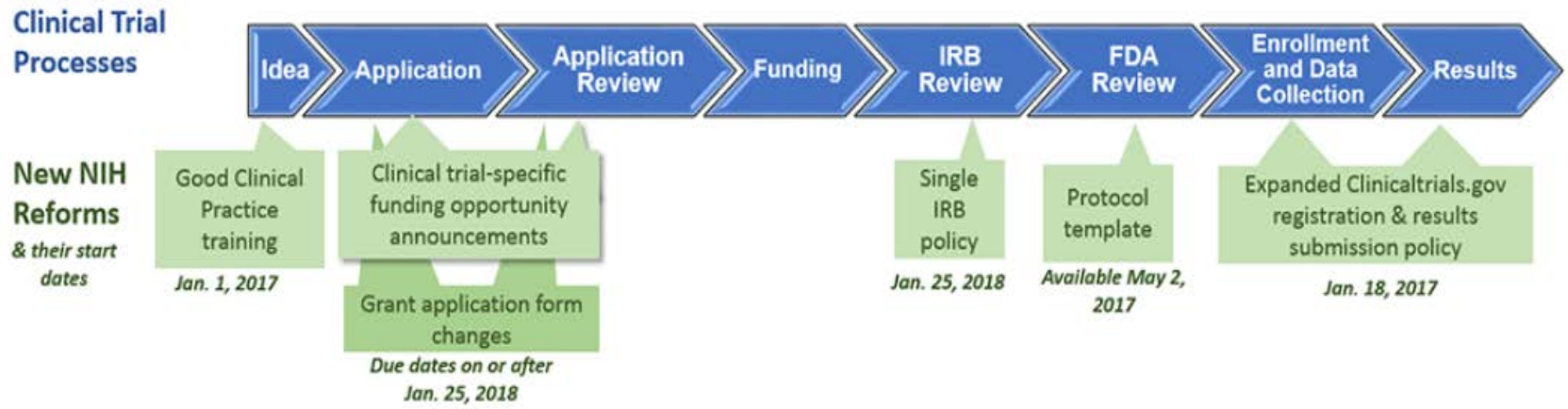
- RFA-AG-18-028
- R01 Clinical Trial Required
- Reissue of RFA-AG-17-059
- Due date: March 26, 2018
- Conduct research involving pragmatic clinical trials into improving the effectiveness of treatment strategies for comorbid conditions that occur frequently in combination with Alzheimer's disease and related dementia (ADRD)
- Phasing is optional
- Uses new clinical trial review criteria

Pragmatic trials for dementia care in long-term services and support settings

- PAR-18-585
- R61/R33 - Clinical Trial Required
- Reissue of RFA-AG-17-065
- Due dates: March 27, 2018; February 20, 2019; and February 20, 2020
- Pragmatic trials for dementia care in LTSS settings designed to address practical comparative questions faced by Alzheimer's disease (AD) and AD-related dementia (ADRD) patients, clinicians and caregivers (both paid and unpaid) and intended to improve quality of care, quality of life, improve cost-effectiveness and reduce disparities
- Pilot research to test the feasibility of implementing and integrating LTSS interventions (R61 phase) that, if successful, can transition to an R33 phase for implementation of large pragmatic trials, using administrative review as basis to advance
- Uses new clinical trial review criteria

NIH clinical trial requirements

- Series of initiatives in 2017-2018 to enhance the accountability and transparency of clinical research
- Clinical Trial-specific Funding Opportunities
- Clinical Trial-specific Review Criteria
- Single IRB requirement



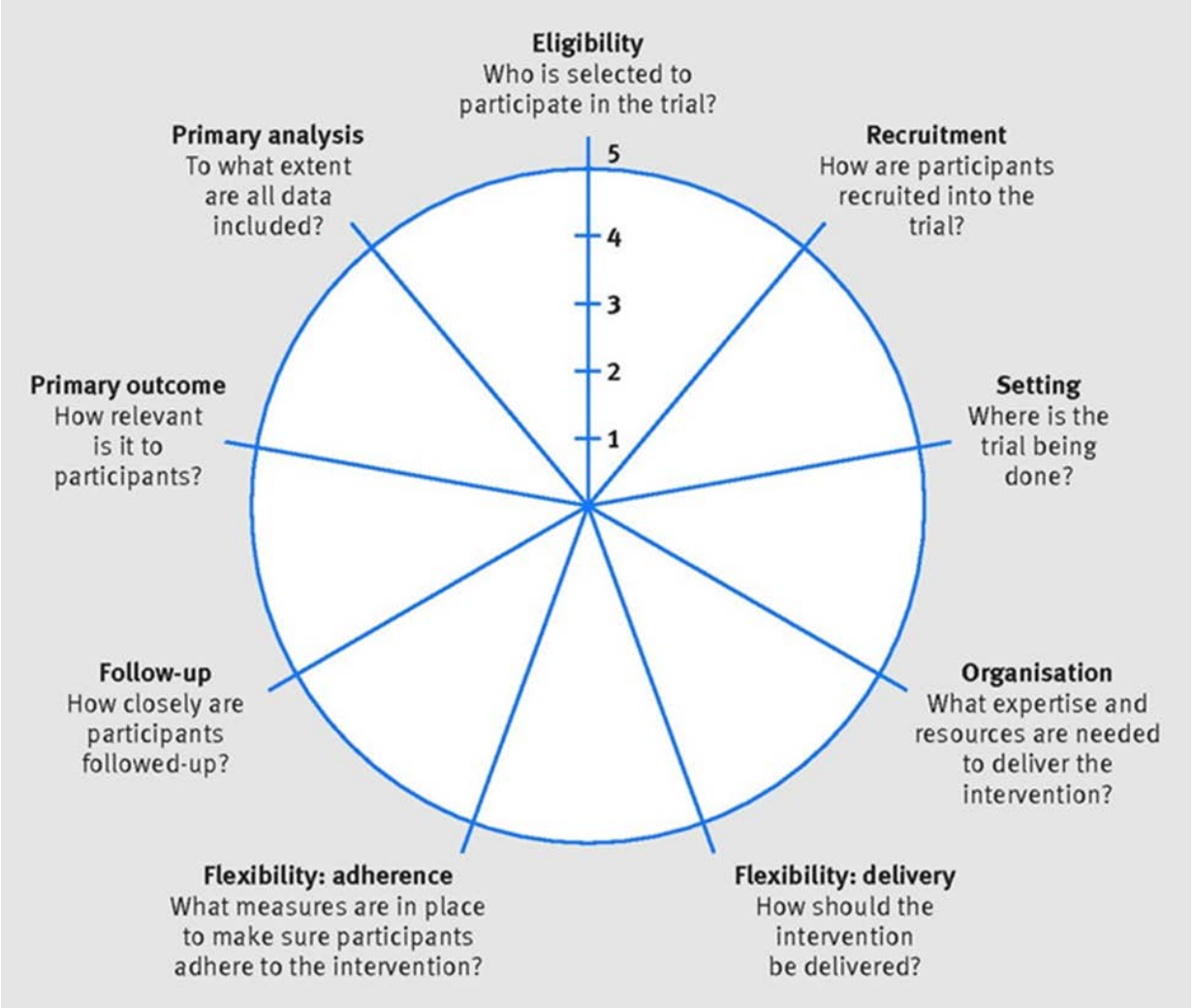
New review criteria—clinical trials

- Application may include study design, methods, and intervention that are not by themselves innovative but address important questions or unmet needs
- Has new questions under each of the standard criteria, in particular the Approach section should address Study Design, Data Management and Statistical Analysis.
- One Additional Review Criteria for **Study Timeline**

  Is the study timeline described in detail, taking into account start-up activities, the anticipated rate of enrollment, and planned follow-up assessment? Is the projected timeline feasible and well justified? Does the project incorporate efficiencies and utilize existing resources (eg, CTSAs, practice-based research networks, electronic medical records, administrative database, or patient registries) to increase the efficiency of participant enrollment and data collection, as appropriate? Are potential challenges and corresponding solutions discussed (eg, strategies that can be implemented in the event of enrollment shortfalls)?

Source: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-118.html

PRECIS-2 domains



Some real (troubling) summary statement comments …

“The premise of the study … is based on weak evidence”

“Data provided did not establish the feasibility of recruitment”

“The differences in anticipated [outcome] rates upon which the study is powered are quite large—larger differences than are seen in other similar trials”

“No adequate description of how activities in the planning phase would inform activities in the implementation phase of the study”

“Concerns include the inclusion/exclusion criteria for the study, inadequate power for the study, and whether outcomes of this study would drive a change in [clinical] practices”

“There are no measures of intervention fidelity”

“Investigative team … had limited experience with multi-systems clinical trials”

“Amount budgeted for a biostatistician is much too low”

Common pitfalls

- Overly ambitious—beyond the life/length of the application
- Missing or inappropriate control groups
- Lack of sufficient expertise or skilled collaborators needed to complete the studies
- Not sufficient publications in the area of proposed studies
- Insufficient statistical power
- Cannot recruit the needed population

Strategies for success

- The research question posed must be clear
- The most elegant methods, techniques, and procedure are worthless if you do not convince the reviewer that the study is worth doing
- High tech is no substitute for solid logical planning
- Sell your research plan–highlight the strengths
- Identify weaknesses & explain how you will deal with them
- Tailor your application to the funding agency
- Obtain feedback of your collaborators, consultants & others

Dos and don’ts

DO

- Justify the research
- Include pilot data
- Address potential overlaps
- Reduce complexity
- Ensure aims are capable of advancing the field
- Choose appropriately expert personnel
- Link data collection & analysis to aims
- Justify use of multiple sites & sample size

Source: https://www.nia.nih.gov/research/blog/2015/01/strengthen-your-research-plan-better-score-dos-and-donts

Dos and don’ts

DON’T

- Skip any steps (eg, literature review)
- Use dense/confusing writing style
- Use appendix inappropriately
- Include untestable aims
- Include non-relevant aims or fishing expeditions
- Assume that prior collaboration is irrelevant

Source: https://www.nia.nih.gov/research/blog/2015/01/strengthen-your-research-plan-better-score-dos-and-donts

NIH Research Methods Resources

Source: https://researchmethodsresources.nih.gov

Discussion questions

- Non-disease vs disease-specific institute?
  - Consult program officers for both
- Single vs multiple PI? Suitability for assist mechanism (U)?
- What materials would be good for training reviewers?
- Other individual questions that might be of more general interest

Important things to know

- Online resources are available for the development of pragmatic trial grant applications
- NIH has new policies & forms related to clinical trial grant applications
- Some things, such as milestones & safety monitoring, may be negotiable around the time of an award

Important things to do

- Read relevant Funding Opportunity Announcement multiple times
- Identify program staff at your target NIH Institute/Center & review your Specific Aims and any questions with them
- Obtain adequate feedback on the Research Plan from the entire team

For further information, contact

Marcel Salive, MD, MPH

301-496-5278

Marcel.Salive@nih.gov

Next steps for your project