Informational Session
RFA-TR-18-20
RFA-TR-18-21
June 27, 2018
Webinar information

All phones will be muted at the beginning of the call to avoid sounds of dogs, cats, kids, airport announcers, sirens and hold music.

If you have questions please type them into the chat box and we will respond during the question and answer period.
# Rare Diseases Clinical Research Network

## 2002
### Beginning
- Rare Diseases Act of 2002
- (Public Law 107-280)
- Established "RDCRC’s of Excellence"

## 2003
### Early Years
- First RFA released
- 7 consortia funded

## 2008 - 2013
### Development
- 2008 – 19
- 20013 – 22
- 31 Individual consortia
- 238 Disorders
- >40,000 Participants

## 2018
### Future
- RFA-TR-18-020
- RFA-TR-18-021
Definitions

RDCRN
Rare Diseases Clinical Research Network

RDCRC
Rare Diseases Clinical Research Consortium

DMCC
Data Management and Coordinating Center

CPAG/PAG
Coalition of Patient Advocacy Groups
The RDCRCs are intended to advance the diagnosis, management, and treatment of rare diseases with a **focus on clinical trial readiness**. Each RDCRC will promote highly collaborative, multi-site, patient-centric, translational and clinical research with the intent of addressing unmet clinical trial readiness needs.
RDCRC vs. RDCRN

Individual Consortium & PAG

Consortium RDCRC

All funded RDCRC, DMCC & PAGs

Network RDCRN
RDCRC Participants

Patients & Patient Advocacy Groups

Researchers & Clinicians

NIH
DMCC Structure

- Clinical Research Support
- Data Standards, Sharing & Storage
- Engagement & Dissemination
- Administrative Support

Consortium Support RDCRC

Network Support RDCRN
Coalition of Patient Advocacy Groups

• Each RDCRC & DMCC Must Actively Engage with Patient and Advocacy Groups
Five Required Sections of an RDCRC Application
Section I - Overall

• Requirements

• This section should describe:
• The major theme of the RDCRC,
• Its goals and objectives,
• Background information, the overall importance of the research and
• Provide a sense of the overall significance of the RDCRC, i.e. how the RDCRC infrastructure and any results and resources it generates will impact the encompassed rare diseases in the near- and long-term if the goals and objectives are achieved.

• Page Limit - 12 Pages
Section 2 - Administrative Core

• Requirements

• The RDCRC Administrative Core is responsible for the overall administration of the RDCRC (including policy, procedure, and funds allocation) and the integration of all activities within and among the RDCRC sites.

• Coordinating communication among the RDCRC sites and integrating participating researchers into a cohesive RDCRC environment

• Point of coordination with the RDCRN via the DMCC and the patient and stakeholder communities.

• The Administrative Core will include:

• A Clinical Team Liaison who is a clinical investigator. The Clinical Team Liaison will ensure a mutually supportive interaction between the scientists conducting clinical research.

• An Administrative Coordinator should be identified in the application who will be responsible for assisting the RDCRC Director (PD/PI of the application) with day-to-day administrative details and program coordination.
Section 2 - Administrative Core (continued)

• Requirements

• The Administrative Core will also coordinate and support RDCRN-wide efforts to develop and monitor best practices for clinical and research data handling and use, including the use of Common Data Elements (CDEs).

• The Administrative Core is expected to establish and maintain a website to communicate the RDCRC mission and the availability of career enhancement opportunities provided through the Career Enhancement Core, and to provide access to information about RDCRN-wide resources provided by the DMCC.
Section 3 - Clinical Research Projects

• Requirements

• The RDCRCs are intended to advance the diagnosis, management, and treatment of rare diseases with a focus on clinical trial readiness.

• A minimum of two but no more than five multi-site clinical research projects are required.

• One of the projects must be longitudinal in nature (e.g., Natural History Studies).

• If a clinical research project is proposed, it need not include an intervention. See Section IV.2 for additional guidance on projects that propose a clinical trial.

• Epidemiological, behavioral and health outcomes research studies in rare diseases are also encouraged.
Section 3 - Clinical Research Projects (continued)

• Requirements

• Each of the proposed clinical research projects should:
  • Address problems that require substantial collaborative research effort and a multi-site RDCRC environment to solve,
  • Benefit from NIH programmatic input,
  • Are more substantial than a stand-alone grant.

• Collectively, the projects should involve synergistic teams with experience in rare diseases or disease/disorder/syndrome/condition/manifestation along with complementary expertise.

• Collaborations should be arranged to bring the best expertise to bear on a problem while ensuring input from all patients and stakeholders (parents, caregivers, support and advocacy groups).

• Page limits 12 pages per research project
Section 4 – Pilot Feasibility Core

• Requirements

• A Pilot/Feasibility Core should be established to enable future innovative single- or multi-site pilot studies aimed at advancing the diagnosis, clinical trial readiness, management and/or treatment of rare diseases.

• Pilot projects that extend RDCRC research collaborations beyond the RDCRN are encouraged.

• Pilot/Feasibility projects must not be described in the current application and if described will not be considered in the review of the application.

• The selection and initiation of future pilot/feasibility projects are contingent upon approval by the NIH and the assigned NIH institute, and are subject to NIH clinical research regulations, see Prior NIH Approval of Human Subjects Research in Active Awards Initially Submitted without Definitive Plans for Human Subjects Involvement (Delayed Onset Awards): Updated Notice https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-129.html
Section 5 - Career Enhancement Core

• Requirements

• Each RDCRC should provide a Career Enhancement Program to provide support for career enhancement-related expenses for:
  • predoctoral,
  • postdoctoral
  • clinical fellow
• Support for activities that enhance the institution's environment for the education of students/post-docs and early-stage investigators in rare diseases research.
• Leveraging existing career enhancement programs and exploring sponsorship opportunities are encouraged.
• This program may propose activities that enhance the career enhancement environment through specialized coursework, a seminar program, retreats for presentation of students/post-doc research, journal clubs or other activities that contribute to the preparation of junior investigators for careers in rare diseases research.
• Exposure to research at other RDCRCs is also encouraged through exchange programs, short-term career enhancement opportunities or visits to learn new research approaches.
Applications Must include

Patient/Stakeholders
3 or More Rare Diseases
Multiple Sites
At least 1 longitudinal study
Clinical Studies
What is a Rare Disease
Occurs in <200,000 people in the United States

Application must include 3 Rare Diseases

Disorders – abnormal physical or mental conditions or ailments

Syndromes – Group of symptoms that occur together. Or a condition characterized by a set of associated symptoms

Diseases – a disorder of structure of function that effects a specific location

Manifestation – symptom or sign of an ailment

Conditions – A particular state of being that limits/restricts something else
NO ANIMAL STUDIES
Single IRBs are required

The applicant is expected to submit a plan describing the use of a Single IRB (sIRB) that will be selected to serve as the IRB of record for all study sites. Are strongly encouraged to use SMARTIRB and its reliance agreements

https://smartirb.org/#
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<th>Renewal Requirements x Years of Support</th>
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<td>The value of continuing ongoing natural history studies with regard to clinical trial readiness</td>
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<td>A timeline that illustrates the transition process and out years beyond NIH funding period</td>
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RDCRC Governance

- External Advisory Committee (EAC)
- Scientific, clinical and patient group representation
- At least 5 members
- Functions in an advisory capacity providing review and critique of program activities
- Must meet at least once a year face-to-face or electronically
- Starts 1\textsuperscript{st} or 2\textsuperscript{nd} year
Data Sharing Within the DMCC

RDCRN participants will be required to share their data within the DMCC

- Advancing rare disease research by freely sharing high-value data is a critical goal of the program.
- Deidentified data collected within this Network and housed within cloud services provisioned by NCATS will become a resource for the greater rare disease research community and will be made available to the scientific community, stakeholders and other relevant partners in a timely manner that meets all NIH human subject's protection, data safety and data sharing requirements.
NCATS Provided Data Management Services via DMCC

RDCRN participants will be required to share their data within the DMCC.
NCATS Cloud & Infrastructure

NCATS provides access and expertise in provisioning, managing, and securing cloud services. NCATS currently has access to services from all major cloud providers for commercial and government cloud environments.
NCATS Federated Access & Authorization

NCATS provides services to identify users and secure access to critical information. NCATS authentication system uses NIH-federated credentials to ensure identity without requiring management of accounts or passwords. NCATS staff maintain, manage, and periodically audit access control to systems or specific resources to meet client needs.

NCATS Federated access services include:

NCATS Authorization services:
- NCATS staff manage access to specific systems
- Granular control of system access
- Quickly and efficient add or remove users or permissions
- Automate services for approved users
NCATS DevOps and cloud engineering staff provide the infrastructure and services needed to quickly develop, test, and deploy applications to the cloud.

NCATS DevOps capabilities:
- Access to continuous integration pipeline infrastructure
- Automated deployments to cloud environments
- On track for FedRAMP ATO

NCATS Cloud Engineering capabilities:
- Cloud architecture and design support
- Security considerations
- Existing cloud infrastructure
- Support for Amazon, Google, and Microsoft cloud environments
- Cloud.gov integrated infrastructure management
RDCRN
Data Management
and Coordinating
Center
What has changed? What hasn’t

What is the same?
• Cooperative Agreement
• Supports multi-component research resource projects and centers that will enhance the capability of resources to serve biomedical research.
• Substantial federal programmatic staff involvement is intended to assist investigators during performance of the research activities, as defined in the terms and conditions of the award

What is different?
• New mechanism – U2C
• Multiple Cores
• The DMCC Data Management Core will provide Cloud Computing Services and Engineering Support provisioned by the Information Resources Technology Branch (ITRB), NCATS
DMCCs role within the RDCRN is threefold:
1. Provide clinical research and data management support to the individual RDCRCs
2. Coordinates activities across the RDCRN and helps establish an identity for the network as a rare diseases resource
3. Serves as a conduit of information related to the rare diseases research being conducted with the network to both the research community and the general public
Required components of RDCRN DCMC

Administrative Core

Clinical Research Core

Data Management Core

Engagement and Dissemination Core
Administrative Core Responsibilities

01. Provide overall coordination for the RDCRN and management of the RDCRN activities including steering committee meetings

02. Provide oversight and ensure coordination of all DMCC Cores

03. Provide support for the CPAG meetings

04. Responsible for the preparation of the annual report for the External Scientific Panel (ESP)
Data Management Core Responsibilities

01 Support and enhance a collaborative informatics community for the RDCRN

A management system for collection, storage, and quality control of clinical research data, including a web-based platform that allows for real-time tracking of data quality and completeness and that facilitates remote monitoring.

02 A portal and tools for research scientists and clinicians to access and manage their own data.

03 A portal and tools to share information both within and outside of the RDCRN in a manner that meets all NIH human subject’s protection, data safety and data sharing requirements.
In collaboration with representatives of the RDCRC, develop and monitor Good Data Practices (GDP) of clinical and research data will assist in facilitating the use of Common Data Elements (CDE).

Coordinate and facilitate data standards across the network.
Clinical Research Core Responsibilities

01
Serve a Network resource, providing expertise and consulting to the RDCRC in areas including but not limited to Protocol Development and Management, Biostatistics, and Study Designs.

02
Provide cutting edge information and guidance for RDCRN member on trans-RDCRN disease related issues (e.g., working with industry, navigating regulatory process).

03
Support in establishing single IRBs.

04
In collaboration with the RDCRCs coordinate training issues that cut across topics relevant to multiple RDCRC sites for RDCRN trainees.
Engagement and Dissemination Core Responsibilities

01 Work collaboratively with the RDCRC and CPAGs will develop a broad outreach program for the Network

02 Outreach will extend to basic and clinical researchers, academic and practicing physicians, patients and the general public

03 Provide an internet-based web-portal to serve as a central access point to information generated by the RDCRCs
The DMCC PD(s)/Pl(s) cannot serve as the Program Director/Principal Investigator of a project in another active RDCRN award.

Cores may be located at different locations as long as there is a strong plan for communication and collaboration.
If DSMB services are required, they may be requested from the DMCC, only if no alternate source exists. To be eligible for the DMCC services clinical trials or pilot studies must be of greater than minimal risk, and include one or more of the following:

Have protocol designs that allow for modifications to the trial or statistical procedures of the trial after its initiation, such as an adaptive design

Evaluate novel technology or an intervention for which prior data (e.g., pre-clinical toxicology or from a related compound) suggest the intervention under study has the potential to induce a potentially severe or unacceptable toxicity

The study is intended to provide definitive information about the effectiveness or safety of the intervention

It would be ethically important to stop the study early if the primary question is addressed, for futility, or for other pre-specified reasons
DMCC Governance

- External Advisory Committee (EAC)
- Scientific, clinical and patient group representation
- At least 5 members
- Functions in an advisory capacity providing review and critique of program activities
- Must meet at least once a year face to face or electronically
- Starts 1st or 2nd year
RDCRN Formation and Governance

- Cooperative agreement = close interaction with NIH
- Governance rests with Network Steering Committee with advice from an External Scientific Panel (ESP)
- Steering committee consists of
  - RDCRC PI(s) & PAG rep
  - DMCC PI(s)
  - NIH Program Directors/Scientists
External Scientific Panel Established by NIH
Please feel free to contact program staff
With any questions you may have.
Tip – send an email and set up a call

- Contact Tiina with any RDCRN/RDCRC/DMCC specific questions
- Contact all relevant ICs (yes there may be more than one) with disease and IC specific questions.
Peer Review
Applications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Groups (s), convened by the National Center for Advancing Translational Sciences in accordance with NIH peer review policy and procedures, using the stated review criteria. Assignments to a Scientific Review Group will be shown in the eRA Commons.

As part of the scientific peer review, all applications:

- May undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review) will be discussed and assigned an overall impact score.
- Will receive a written critique.
Potential Review Meeting Formats

Virtual Meeting
Teleconference
Face-to-face
Hybrid
Reviewers

Recruitment based on:
Expertise (includes broad experience managing complex clinical trials)
Stature in field
Impartiality
Ability to work in a group
Managed conflicts of interest
Availability
Conflict of Interest – off the panel

Proposed reviewer may not be on the study section if:
• The reviewer is named on the application in a major professional role
• The reviewer is a member of an NIH Advisory Council
• The reviewer (or close family member) would receive a direct financial benefit if the application is funded

Conflict of Interest – out of the room

Proposed reviewer may **be on** the study section but **may not** review certain applications and must leave the room when:

- The PI or others on the application with a major role are from the reviewer’s institution or institutional component (e.g., department)
- Within the past three years, the reviewer has been a collaborator or has had any other professional relationship (e.g., served as a mentor) with any person on the application who has a major role
- The application includes a letter of support or reference letter from the reviewer
- The reviewer serves as a member of the advisory board for the project under review
- The reviewer has an indirect financial interest from the applicant institution or PD/PI of over $10,000 in honoraria, stocks, and fees during the course of the last year or during the project period

e.g. **Reviewers are instructed to:** Score an application as presented in its entirety. You may not modify your scores on the assumption that a portion of the work proposed will be deleted or modified according to the SRG’s recommendations.
How eRA Assembles Multi-project Applications

https://grants.nih.gov/grants/electronicreceipt/files/Electronic_Multi-project_Application_Image_Assembly.pdf

Reviewers receive the same image (PDF) that the PI receives.
Application Submission
Effort – Per the FOA

The minimum cumulative effort of the principal investigator(s) of a consortium should be at least 2.1 person months per year.

The cumulative effort of the Principal investigator(s) should be at minimum 2.1 person months per year.

No minimum is specified for Project Lead or Core Leads.
## Page Limits – Per the FOA


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<thead>
<tr>
<th>Component Types Available in ASSIST</th>
<th>Research Strategy/Program Plan Page Limits</th>
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<tbody>
<tr>
<td>Overall</td>
<td>12 pages</td>
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<tr>
<td>Admin Core</td>
<td>6 pages</td>
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<td>Clinical Res Project</td>
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<td>Career Enhancement</td>
<td>6 pages</td>
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## Page Limits – More detail per NIH Website


<table>
<thead>
<tr>
<th>Section of Application</th>
<th>Activity Codes</th>
<th>Page Limits * (if different from FOA, FOA supersedes)</th>
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<tbody>
<tr>
<td>Project Summary/Abstract</td>
<td>For all Activity Codes</td>
<td>30 lines of text</td>
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<tr>
<td>Project Narrative</td>
<td>For all Activity Codes excluding C06, UC6 and G20.</td>
<td>three sentences</td>
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<tr>
<td>Specific Aims</td>
<td>For all Activity Codes that use an application form with the Specific Aims section (including each component of a multi-component application)</td>
<td>1</td>
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</tbody>
</table>
How to apply – Application Guide

The R&R Other Project Information Form is used for all grant applications. This form includes questions on the use of human subjects, vertebrate animals, and environmental impact. This form also has fields to upload an abstract, project narrative, references, information on facilities, and equipment lists.
Using the PHS Human Subjects and Clinical Trials Information form:

Follow instructions on the PHS Human Subjects and Clinical Trials Information form that are specific to your answer to the “Are Human Subjects Involved?” question on the M.220 - R&R Other Project Information Form. The PHS Human Subjects and Clinical Trials Information form allows you to add study record(s) and/or delayed onset study(ies), as applicable.

Within each Study Record: PHS Human Subjects and Clinical Trials Information, you will add detailed information at the study level. Add a separate study record for each protocol involving human subjects proposed in your application. Do not duplicate studies within your application. Each study within the application should be unique and should have a unique study title.
Tips for Describing Human Subjects Studies in Multi-project Applications


If work on the same study spans multiple components, then include the details for the study in the Overall component to avoid duplication. When completing the PHS Human Subjects and Clinical Trials Information form in the Overall component, complete a full or delayed onset study record and use the Other Requested Information Attachment to identify the components in which the work is being done. When completing the PHS Human Subjects and Clinical Trials Information form in the components working on the study, use the Other Requested Information attachment to indicate the study details are included in the Overall component.
Progress Report for Renewal and Revision Applications

Note that the Progress Report falls within the Research Strategy and is therefore included in the page limits for the Research Strategy.
For renewal/revision applications, provide a Progress Report. Provide the beginning and ending dates for the period covered since the last competitive review. In the Progress Report, you should:
• Summarize the specific aims of the previous project period and the importance of the findings, and emphasize the progress made toward their achievement.
• Explain any significant changes to the specific aims and any new direction, including changes resulting from significant budget reductions.
• Discuss previous participant enrollment (e.g., recruitment, retention, inclusion of women, minorities, children, etc.) for any studies meeting the NIH definition for clinical research.
• Use the Progress Report section to discuss, but not duplicate information collected elsewhere in the application.
Do not include a list of publications, patents, or other printed materials in the Progress Report. That information will be included in the “Progress Report Publication List” attachment.
Progress Report Publication List

Who must complete the “Progress Report Publication List” attachment:

A “Progress Report Publication List” attachment is required only if the type of Application is renewal.

Descriptions of different types of applications are listed in NIH’ Types of Applications

Format:
Attach this information as a PDF file. See NIH’s Format Attachments page.
Consortium/Contractual F&A Costs:

<table>
<thead>
<tr>
<th>F. Other Direct Costs</th>
<th>Funds Requested ($)</th>
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<tbody>
<tr>
<td>1.  Materials and Supplies</td>
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<td>2.  Publication Costs</td>
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<td>3.  Consultant Services</td>
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<td>4.  ADP/Computer Services</td>
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<td>5.  Subawards/Consortium/Contractual Costs</td>
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<td>6.  Equipment or Facility Rental/User Fees</td>
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<td>7.  Alterations and Renovations</td>
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Total Other Direct Costs
5. Subawards/Consortium/Contractual Costs:
List the total funds requested for:
   all subaward/consortium organization(s) proposed for the project and
   any other contractual costs proposed for the project.
This line item should include both direct and indirect costs for all subaward/consortium organizations.
NIH policy provides for the exclusion of consortium/contractual F&A costs when determining if an applicant is in compliance with a direct cost limitation. However, you must include the full cost of subaward/consortium in the Subawards/Consortium Costs field (M.300 - R&R Budget Form, Section F. Other Direct Costs, Question 5).
Letters should stipulate expectations for co-authorship, and whether cell lines, Samples or other resources promised in the letter are freely available to other Investigators in the scientific community or will be provided to the particular Investigators only.

For consultants, letters should include rate/charge for consulting services and level of effort/number of hours per budget period anticipated. In addition, letters ensuring access to core facilities and resources should stipulate whether access will be provided as a fee-for-service.

Letters are not required for personnel (such as research assistants) not contributing in a substantive, measurable way to the scientific development of execution of the project.
Peer Review Contact Information

Peer Review Contact(s)
B. Duane Price, Ph.D.
National Center for Translational Sciences (NCATS)
Telephone: 301-435-0829
Email: b.duane.price@nih.gov
Frequently Asked Questions
Questions (1, 2):

1. It is the intent of the NIH to not support individual RDCRCs for more than 15 years (three awards) after awards are made under this FOA. As such, may a grantee who has been funded for three awards still apply?
   • Yes. All applicants are eligible to apply to this FOA and to be considered for funding. At the end of the funding cycle of awards made under this FOA, applicants with three or more consecutive award segments (which likely equates to 15 or more years of funding) will not be eligible to apply or receive further support under this FOA.

2. Duration of funding will be determined by the “grant number." What is the grant number?
   • The grant number is the number that is assigned to a grant upon initial submission of the application. The serial number (underlined as follows) of the grant does not change through the life of the grant - 5 U54 TR 123456 - 15. The support years (underlined as follows) do change 5 U54 TR 123456 15. This number indicates the grant is in its fifteenth year of support. Please reference the following URL for tips on how to decipher NIH grant numbers: https://era.nih.gov/sites/default/files/Deciphering_NIH_Application.pdf (link is external).
Questions (3, 4):

3. RDCRC budgets should include travel and compensation for EAC. What is allowable? Honorarium? Consulting fees?
   • External Advisory Committee members may receive compensation for their travel and time devoted to the proposed award activity. Funding support requested must be justified. All applicants are requested to work with their Office of Sponsored Programs for determining the most appropriate type of compensation based on their institutional policies and NIH Grants Policy.

4. We are applying for a continuation of our current grant which has a 26% IDC rate, can that rate be used in the renewal request?
   • In accordance with NIH policy and the SF424 instructions, applicants should use their most recently established indirect cost rate in competing and renewal applications.
Questions (5, 6):

5. **What is “clinical trial readiness”?**
   - Different groups may be at differing levels of scientific maturity within their research programs therefore, different studies may be needed to move closer to be ready to conduct clinical trials in the near or distant future. For the purposes of this RFA clinical trial readiness includes studies that validate clinical research tools that can include biomarkers or clinical outcome assessment measures that are fit-for-purpose within a defined context of use relevant to the clinical trials. Clinical trial readiness studies may also propose to expand the knowledge of disease natural history necessary for clinical trial design and can include characteristics for stratification or determining inclusion and exclusion criteria; the stage of disease progression that may be responsive to treatment; and data needed for determining sample size through power calculations.

6. **What is a clinical trial liaison?**
   - The Administrative Core will have a Clinical Team Liaison. This individual will be a trained clinical investigator that will ensure a mutually supportive interaction between the scientists (who are often located at different sites) conducting clinical research.
Questions (7):

7. Do we need letters of support for each section or could we have one broad letter that covers all sections?
Multi-Project (M) Instructions in the SF424 (R&R) Application Guide provide important information regarding the content of the letters. The letter should clearly state what is being provided. Please follow the instructions in the FOA regarding placement of the letters. Note that reviewers are assigned to individual components. Reviewers will be instructed to check the overall section for any letters “missing” from that component.


(Overall) Letters of Support: Applicants must provide letters from the appropriate high-ranking institutional official(s) from the lead institution and partnering institutions that....

(Administrative Core) Letters of Support: Only letters of support specific to the Administrative Core should be attached to this section.

(Clinical Research Project) Letters of Support: Only letters of support specific to each Clinical Research Project should be attached to this section. Provide letters of collaboration from individuals who will contribute in a substantive, meaningful way to the scientific development or execution of the clinical research project, whether or not salaries are requested.

(Pilot/Feasibility Core) Letters of Support: Only letters of support specific to the Pilot/Feasibility Core should be attached to this section. Letters from high-level institution official(s) (e.g., Dean of the School of Medicine, President, and Vice President for Research) should state the institutional support. There is no cost sharing requirement under this FOA. Indication of institutional commitment to the success of the program will be considered positively in the programmatic evaluation of applications. Examples for such support may include ensuring adequate access to facilities.

(Career Enhancement Core) Letters of Support: Only letters of support specific to the Career Enhancement Core should be attached to this section. Letters from high-level institution official(s) (e.g., Dean of the School of Medicine, President, and Vice President for Research) should state the institutional support. There is no cost sharing requirement under this FOA. Indication of institutional commitment to the success of the program will be considered positively in the programmatic evaluation of applications. Examples for such support may include ensuring adequate access to facilities.
8. Is the Career enhancement just for pre-docs?
   • Per the FOA, each RDCRC should provide a Career Enhancement Program to provide support for career enhancement-related expenses for predoctoral, postdoctoral and/or clinical fellow as well as support for activities that enhance the institution's environment for the education of students/post-docs and early-stage investigators in rare diseases research.

9. Does “pre-doc” include either MDs and PhDs?
   • Both Ph.D.s and MDs may be included

10. Will the External Advisory Committee be convened (and budgeted for) by the RDCRN? Will the External Scientific Panel be convened by NCATS? Should we include compensation for the ESP members in our RDCRC budget?
    • The External Advisory Committee (EAC) will be convened and budgeted for by the individual RDCRC. Per both FOAs, The EAC should meet in-person or electronically at least once a year, beginning in the first or second year of the award.
      The External Scientific Panel (ESP) will be convened by NIH program officials. Per both FOAs, the ESP will be named by NIH program officials and will serve in advisory capacity by reviewing RDCRN activities and making recommendations to the Network Steering Committee and the NIH regarding process and substantive issues that arise during Network operations.
11. What can be included in the Appendix?

Per FOA RFA-TR-18-021 & RFA-TR-18-020: Limited items are allowed in the Appendix. Follow all instructions for the Appendix as described in the SF424 (R&R) Application Guide; any instructions provided here are in addition to the SF424 (R&R) Application Guide instructions.


Beginning with applications submitted to the NIH, AHRQ, or NIOSH for due dates on or after January 25, 2018, unless specified otherwise in the FOA, the only allowable Appendix materials are:

- Blank data collection forms, blank survey forms and blank questionnaire forms -- or screenshots thereof.
- Simple lists of interview questions. For clarification, these blank forms and lists are not and do not include items such as: data, data compilations, lists of variables or acronyms, data analyses, publications, manuals, instructions, descriptions or drawings/figures/diagrams of data collection methods or machines/devices.
- Blank informed consent/assent forms

Other items only if they are specified in the FOA as allowable Appendix materials

Some FOAs further restrict allowable appendix materials and/or may specify that some materials listed above must be provided in another part of the application. Applications submitted to those FOAs must follow instructions in the FOA and must not put those items in the Appendix.

No other items are allowed in the Appendix. Simply relocating disallowed materials to other parts of the application will result in a noncompliant application unless they are items specified in the FOA as optional or required for those other sections of the application.

Consequence for Submitting Disallowed Materials:

Applications submitted for due dates on or after January 25, 2018 will be withdrawn as noncompliant if they are submitted with Appendix materials that are not specified in this Notice or specified in the individual FOA as allowed or required.
Questions (12, 13):

12. Will we be able to use DMCC auditors to provide quality control of on-going research?
   • Please review the DMCC RFA-TR-18-021. Audits are no longer a function of the DMCC.

13. It appears the RDCRN DMCC will no longer convene the DSMB?
   • Per both FOAs, if DSMB services are required, they may be requested from the DMCC, only if no alternate
     source exists, for RDCRC clinical trials or pilot studies that meet program requirements. To be eligible for the
     DMCC services clinical trials or pilot studies must be of greater than minimal risk.

     The RDCRN will only provide DSMB services in the following circumstances.
     
     If DSMB services are required, they may be requested from the DMCC only if no alternate source exists. To
     be eligible for the DMCC services, clinical trials or pilot studies must be of greater than minimal risk, and
     include one or more of the following:

     1) Protocol designs that allow for modifications to the trial or statistical procedures of the trial after its
        initiation, such as an adaptive design;

     2) Plan to evaluate novel technology or an intervention for which prior data (e.g., pre-clinical toxicology or
        from a related compound) suggest the intervention under study has the potential to induce a potentially
        severe or unacceptable toxicity;

     3) Objective to provide definitive information about the effectiveness or safety of the intervention (e.g., a
        Phase 3 or efficacy trial, such as a trial intended to support product registration);

     4) Ethics-driven need to stop the study early if the primary question is addressed, for futility, or for other pre-
        specified reasons.
Questions (14, 15):

14. In the Career Enhancement Core language, specifically what is meant by the support of those besides the fellows, such as the students?
   • This program may propose activities that enhance the career enhancement environment through specialized coursework, a seminar program, retreats for presentation of students/post-doc research, journal clubs or other activities that contribute to the preparation of junior investigators for careers in rare diseases research. Exposure to research at other RDCRCs is also encouraged through exchange programs, short-term career enhancement opportunities or visits to learn new research approaches.

15. Regarding single IRB- Does the reliance have to be with the same IRB across all projects?
   • No different sites may serve as the central IRB for different projects however, each project should have a single IRB.
Timeline

- **RFA’s Released**: TR-18-020, TR-18-021
  - June 8, 2018
- **Informational Session I**: TR-18-029
  - June 27, 2018
- **Informational Session II**: TR-18-029
  - July 19, 2018
- **Application Due Date**: Due by 5:00 PM local time of applicant organization
  - Oct. 9, 2018
- **Scientific Review**
  - @ NCATS
  - Feb. 2019
- **Advisory Council**
  - @ Funding institutes
  - May 2019
- **Earliest Start Date**: July 2019