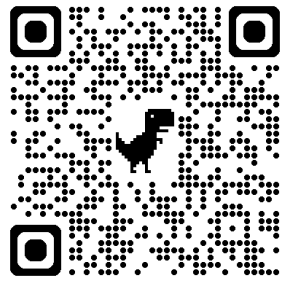# Webinar Information

- All external participants will be muted during the webinar
- If you have questions during the webinar, please submit them to
    - NCATS_RDCRN@mail.nih.gov
- Questions that are specific to your application/science will not be answered during the webinar.
- Answers to questions not addressed during the webinar will be provided on the NCATS RDCRN Applicant Information page:
    - https://ncats.nih.gov/research/research-activities/RDCRN/applicant-information

- Automated captions are available during this webinar by clicking the 'Show captions' icon on your Zoom toolbar. Please contact NCATS_RDCRN@mail.nih.gov or 301-827-2746 if you require assistance.
- Sign language interpreting and real-time captioning services are available upon request for the June 3rd session of this webinar.
- Individuals requiring either of these services and/or other reasonable accommodation, please contact Chris Maurer at christopher.maurer2@nih.gov or 301-827-7280 by Friday, May 24.

Rare Diseases Clinical Research Consortia (RDCRC) for the Rare Diseases Clinical Research Network (RDCRN) (U54 Clinical Trial Optional)

PAR-24-206

Tiina K. Urv, Ph.D.
Program Director

Division of Rare Diseases Research Innovation (DRDRI)
National Center for Advancing Translational Sciences (NCATS)

Definitions

- **RDCRN** = Rare Diseases Clinical Research Network
- **RDCRC** = Rare Diseases Clinical Research Consortium
- **DMCC** = Data Management and Coordinating Center
- **CPAG** = Coalition of Patient Advocacy Groups
  - **PAG** = Patient Advocacy Group(s)
- **NIH** = National Institutes of Health
  - **ICO** = Institute/Center/Office
  - **PO** = Program Official
  - **PS** = Project Scientist
- **PD/PI** = Program Director(s)/Principal Investigator(s)

History of the RDCRN

Rare Diseases Clinical Research Network

- Established by Rare Diseases Act of 2002 (Public Law 107-280)
  - "planning, establishing, or strengthening, and providing basic operating support for **regional centers of excellence** for clinical research into, training in, and demonstration of diagnostic, prevention, control, and treatment methods for rare diseases"
- Established 2003
- Recompeted every 5 years

Funded RDCRC 2003-2024

Consortium Name	RDCRN1 2003-2008	RDCRN2 2009-2013	RDCRN3 2014-2018	RDCRN4 2019-2024
Genetic Disorders of Mucociliary Clearance Consortium (**GDMCC**)	X	X	X	X
Urea Cycle Disorders Consortium (**UCDC**)	X	X	X	X
Vasculitis Clinical Research Consortium (**VCRC**)	X	X	X	X
Porphyrias Consortium (**PC**)		X	X	X
North American Mitochondrial Disease Consortium (**NAMDC**)		X	X	X
Dystonia Coalition (**DC**)		X	X	X
Brain Vascular Malformation Consortium (**BVMC**)		X	X	X
Nephrotic Syndrome Study Network (**NEPTUNE**)		X	X	X
Primary Immune Deficiency Treatment Consortium (**PIDTC**)		X	X	X
Inherited Neuropathy Consortium (**INC**)		X	X	X
Lysosomal Disease Network (**LDN**)		X	X	X
Clinical Research in ALS and Related Disorders for Therapeutic Development (**CReATe**)			X	X
Brittle Bone Disorders Consortium (**BBDC**)			X	X
Consortium of Eosinophilic Gastrointestinal Disease Researchers (**CEGIR**)			X	X
Developmental Synaptopathies Consortium (**DSC**)			X	X
Phenylalanine Families and Researchers Exploring Evidence (**PHEFREE**)				X
Myasthenia Gravis Rare Disease Network (**MGNet**)				X

Ref: Lumsden and Urv. Ther Adv Rare Dis. 2023

Funded RDCRC 2003-2024 continued

Consortium Name	RDCRN1 2003-2008	RDCRN2 2009-2013	RDCRN3 2014-2018	RDCRN4 2019-2024
Congenital and Perinatal Infections Consortium (**CPIC**)				X
Frontiers in Congenital Disorders of Glycosylation (**FCDGC**)				X
Global Leukodystrophy Initiative Clinical Trials Network (**GLIA-CTN**)				X
Rett Syndrome, MECP2 Duplications, and Rett-related Disorders Consortium (**RTT**)	X	X	X	
Rare Kidney Stone Consortium (**RKSC**)		X	X	
Sterol and Isoprenoid Diseases Consortium (**STAIR**)		X	X	
Autonomic Disorders Consortium (**ADC**)		X	X	
Rare Lung Diseases Consortium (**RLDC**)	X		X	
Advancing Research and Treatment for Frontotemporal Lobar Degeneration Consortium (**ARTFL**)			X	
Clinical Investigation of Neurologic Channelopathies (**CINCH**)	X	X		
Salivary Gland Carcinomas Consortium (**SGCC**)		X		
Chronic Graft Versus Host Disease Consortium (**cGVHD**)		X		
Bone Marrow Failure Consortium (**BMFC**)	X			
Rare Genetic Steroid Disorders Consortium (**RGSDC**)	X			
Rare Thrombotic Diseases Consortium (**RTDC**)	X			
Cholestatic Liver Disease Consortium (**CLiC**)	X			

Ref: Lumsden and Urv. Ther Adv Rare Dis. 2023

Network of Consortia

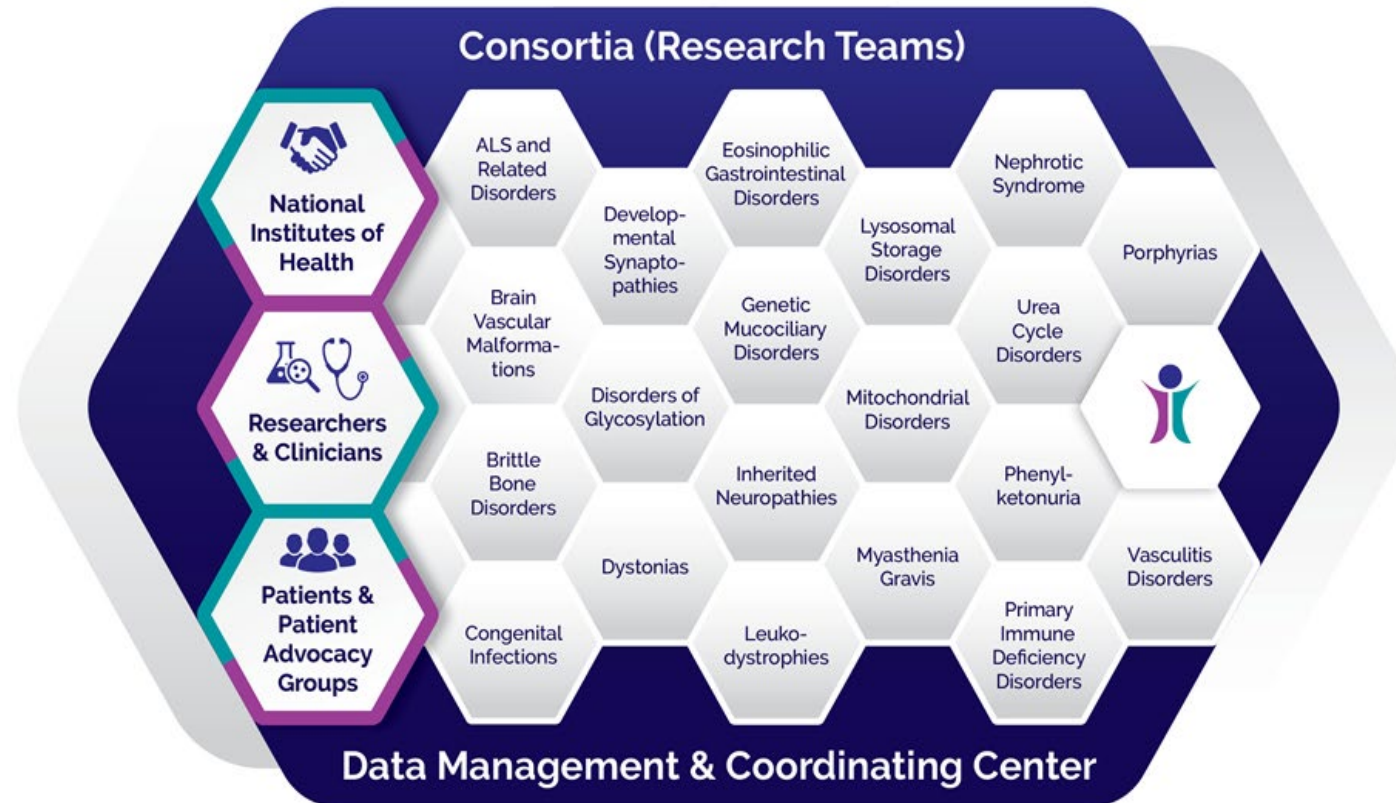| RDCRC	versus	RDCRN
• PIs and team members specific to RDCRC	**Investigators**	• All PIs **and** team members of **all** RDCRCs • The PI(s) from each consortia serves on RDCRN steering committee
• PAG(s) specific to the RDCRC	**Patient Advocacy**	• PAGS from all consortia – Make up the CPAG • One representative from each RDCRC serves on the CPAG steering committee.
• RDCRC-specific NIH Program Official and Project Scientist	**NIH**	• All participating NIH Program Officials and Project Scientists
• DMCC staff assigned specifically to support RDCRC specific activities	**DMCC**	• DMCC staff assigned to support cross network activities

National Center for Advancing Translational Sciences

RDCRN 2019-2024

- A network of 20 research teams collaborating together to achieve faster diagnosis and better treatments for patients with rare diseases

  - NCATS
  - NINDS
  - NIAID
  - NIDDK
  - NICHD
  - NIAMS
  - NHLBI
  - NIDCR
  - NIMH
  - ODS

Notice of Funding Opportunity General Information

https://grants.nih.gov/grants/guide/pa-files/PAR-24-206.html

Objective of Funding Opportunity

- The RDCRCs are intended to advance and improve diagnosis, management, and treatment of numerous, diverse rare diseases through highly collaborative, multi-site, patient-centric, translational, and clinical research.

- **Special emphasis will be placed on the early and timely identification of individuals with rare diseases and clinical trial readiness.**

Clinical Trial Readiness

- For this NOFO, clinical trial readiness is the state of having validated clinical research tools and sufficient knowledge of disease natural history to design efficient clinical trials.

Participating NIH Organizations

- National Center for Advancing Translational Sciences (NCATS)
- National Heart, Lung, and Blood Institute (NHLBI)
- **National Human Genome Research Institute** (NHGRI)
- **National Institute on Aging** (NIA)
- National Institute of Allergy and Infectious Diseases (NIAID)
- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
- Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
- **National Institute on Deafness and Other Communication Disorders** (NIDCD)
- National Institute of Dental and Craniofacial Research (NIDCR)
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
- National Institute of Neurological Disorders and Stroke (NINDS)

# Application Timeline

Letter of Intent	Application Due Date	Scientific Merit Review	Advisory Council Review	Earliest Start Date
July 13, 2024	**August 13, 2024**	**~February 2025**	**~ May - June 2025**	**~July - August 2025**
30 Days Prior to submission Optional	**New and Renewal Application**	**NCATS Managed Review**	**Date is dependent on NIH Institute/Center(s) Council Date**	**Date may vary based on the NIH Institute/ Center(s) Council Review Date**

- All applications are due by 5:00 PM local time of applicant organization.
- Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.
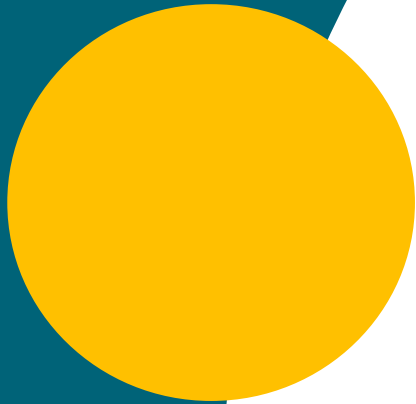
National Center for Advancing Translational Sciences

Eligibility

Eligible Individuals (Program Director(s)/Principal Investigator(s)

- Any individual(s) with the **skills, knowledge, and resources** necessary to carry out the proposed research as the PDs/PIs is invited to work with his/her organization to develop an application for support.

- Individuals from **diverse backgrounds**, including underrepresented racial and ethnic groups, individuals with disabilities, and women are always encouraged to apply for NIH support.

- Individuals should have **documented experience in conducting research** on a disorder that qualifies as **a rare disease** (within the definition of this NOFO).

- Individuals must have **demonstrated experience in managing large multi-component clinical research programs.**

- Multiple PD/PI are allowed.
  - Minimum effort should be at least 2.0 person months per year.
  - If there are multiple PD/PI each individual must meet the minimum requirements.

- The RDCRC PD/PI cannot serve as the PD/PI of a project in another active RDCRC at the time of award, however collaborations among RDCRCs are encouraged.

Eligible Organizations

- Higher Education Institutions
- Nonprofits Other Than Institutions of Higher Education
- For-Profit Organizations
- Local Governments
- Federal Governments
- Other
    - Independent School Districts
    - Public Housing Authorities/Indian Housing Authorities
    - Native American Tribal Organizations (other than Federally recognized tribal governments)
    - Faith-based or Community-based Organizations
   - Regional Organizations

Foreign Organizations

- Non-domestic (non-U.S.) Entities (Foreign Organization) **are not** eligible to apply.

- Non-domestic (non-U.S.) components of U.S. Organizations **are not** eligible to apply.

- Foreign components, as defined in the NIH Grants Policy Statement, **are** allowed.

Foreign Component

- NIH defines a "foreign component" as the performance of any significant element or segment of the project outside the United States either by the grantee or by a researcher employed by a foreign institution, **whether or not grant funds are expended**.

- [NIH Grants Policy Statement Definition of Terms](#)
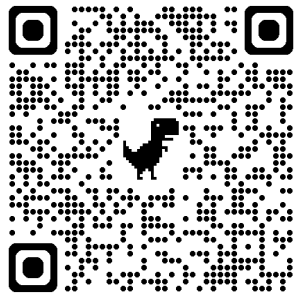
Applications Involving the NIH Intramural Research Program

- NIH Intramural scientists will be limited to the incremental costs required for participation.

- Extramural application include the collaboration with an intramural NIH scientist, no funds for the support of the intramural scientist may be requested in the application.

- The intramural scientist may submit a separate request for intramural funding as described in detail in the NOFO.
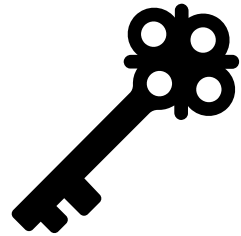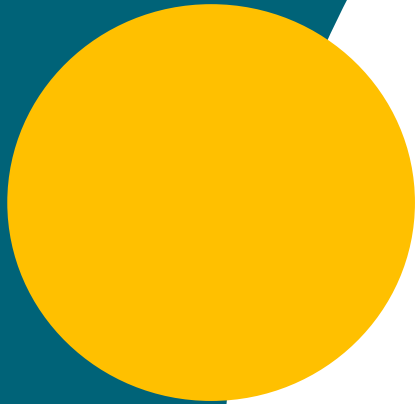
🗝 Key Required Components

Rare Disease

- Each RDCRC application must indicate **at least three different rare diseases** that may share, but are not limited to, common pathways/mechanisms of action/organ system, and may be defined as:
  - **Conditions** - a particular state of being that limits/restricts something else.
  - **Disorders** - abnormal physical or mental conditions or ailments.
  - **Syndromes** - a group of symptoms that occur together, or a condition characterized by a set of associated symptoms.
  - **Diseases** - a disorder of structure or function that affects a specific location and is not simply a result of physical injury.

Other Attachments:
Justification for Rare Disease Status (Required)

- The Rare Disease Status attachment may be no more than **3 pages** in length and must include all targeted diseases/conditions.

- In an "Other Attachment" entitled "Rare Disease Status", all applicants must include a justification that the diseases/conditions being studied are rare in the U.S.

- This section may include one or more references confirming that the prevalence of the diseases/conditions that are the primary focus of the research application is 200,000 or fewer patients in the U.S., as defined by The Rare Diseases Act of 2002 (Public Law 107-280).

- If the diseases/conditions have been granted orphan status by the FDA, provide this information in the justification.

- If it is a rare variant or subset of a more common condition, provide a justification for including this variant in the RDCRC.
  - Describe the scientific basis for separating biomarker/clinical outcome assessment (COA) validation for this rare variant or subset from that of the common condition.

- **Applications missing a Justification for Rare Disease Status may be deemed incomplete and not sent forward for review.**

Clinical Research Studies

- Each RDCRC must have 2 to 4 clinical research studies.

- Each RDCRC is required to have one natural history or longitudinal study.

- Research studies **must all be conducted at multiple sites;** however, future pilot studies may be single site projects.

- Applicants are encouraged to emphasize new ideas, novel approaches, and state-of-the-art technologies to address the needs for early diagnosis and effective treatments along with other strategies to improve the lives of individuals with rare diseases.

Stage of Research Agenda

- Applicants with research agendas at varying stages of scientific development within the research program are encouraged to apply.

- This includes groups that would be considered early-stage RDCRC with many knowledge gaps that need to be addressed
  - e.g., groups that do not yet have established registries, groups with poorly defined natural history data that would benefit from an RDCRC effort.

Coalition of Patient Advocacy Groups (CPAG)

- The RDCRN CPAG was established to promote collaboration between rare disease patient and stakeholder organizations and the RDCRN to facilitate better access to, and earlier benefit from, research conducted on rare diseases.

- **Each RDCRC must form partnerships with patient advocacy groups.** These groups must participate as active members of the RDCRC with meaningful roles within the RDCRC and as members of the RDCRN CPAG.

Single IRB Requirements

- Single IRBs are required for all multisite projects.

- Investigators are strongly encouraged to use SMART IRB and reliance agreements.

- https://smartirb.org
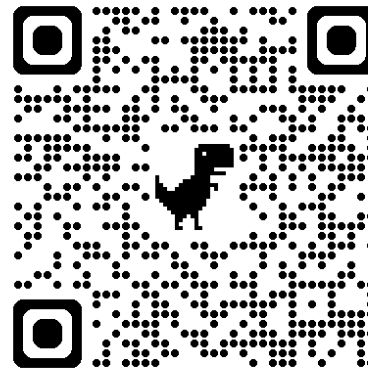
Applications NOT RESPONSIVE to this NOFO

- Single site clinical studies

- Phase III Clinical Trials as part of Clinical Research Projects

- Fewer than three rare diseases included

- There is not at least one longitudinal study

- There are either less than two or more than four research projects submitted

- There is no patient advocacy group involved

- Basic sciences studies
  - Applications that propose any type of animal studies within the RDCRC. The use of in vitro models must be relevant to clinical endpoints (i.e., testing drugs, validating biomarkers versus more basic research)

Up to Three Cycles of Support

- The previous iteration of the RDCRC ([RFA-TR-18-020](#)) indicated that it is the intent of the NIH to support individual RDCRCs for no more than three award cycles; that is, RDCRCs that have successfully competed for RDCRC funding with the same focus three times.

- **New applications should not replicate the research project or aims of the previously funded RDCRC.**

- The NIH will continue to support RDCRCs funded under previous, current, or future funding opportunities for no more than three award cycles.

- **All new projects must address the specific interests of one or more NIH Institute or Center.**

- Prospective applicants are strongly encouraged to consult with the Scientific/Research Contacts of the NIH early in the preparation of the application (see Section VII. Agency Contacts).
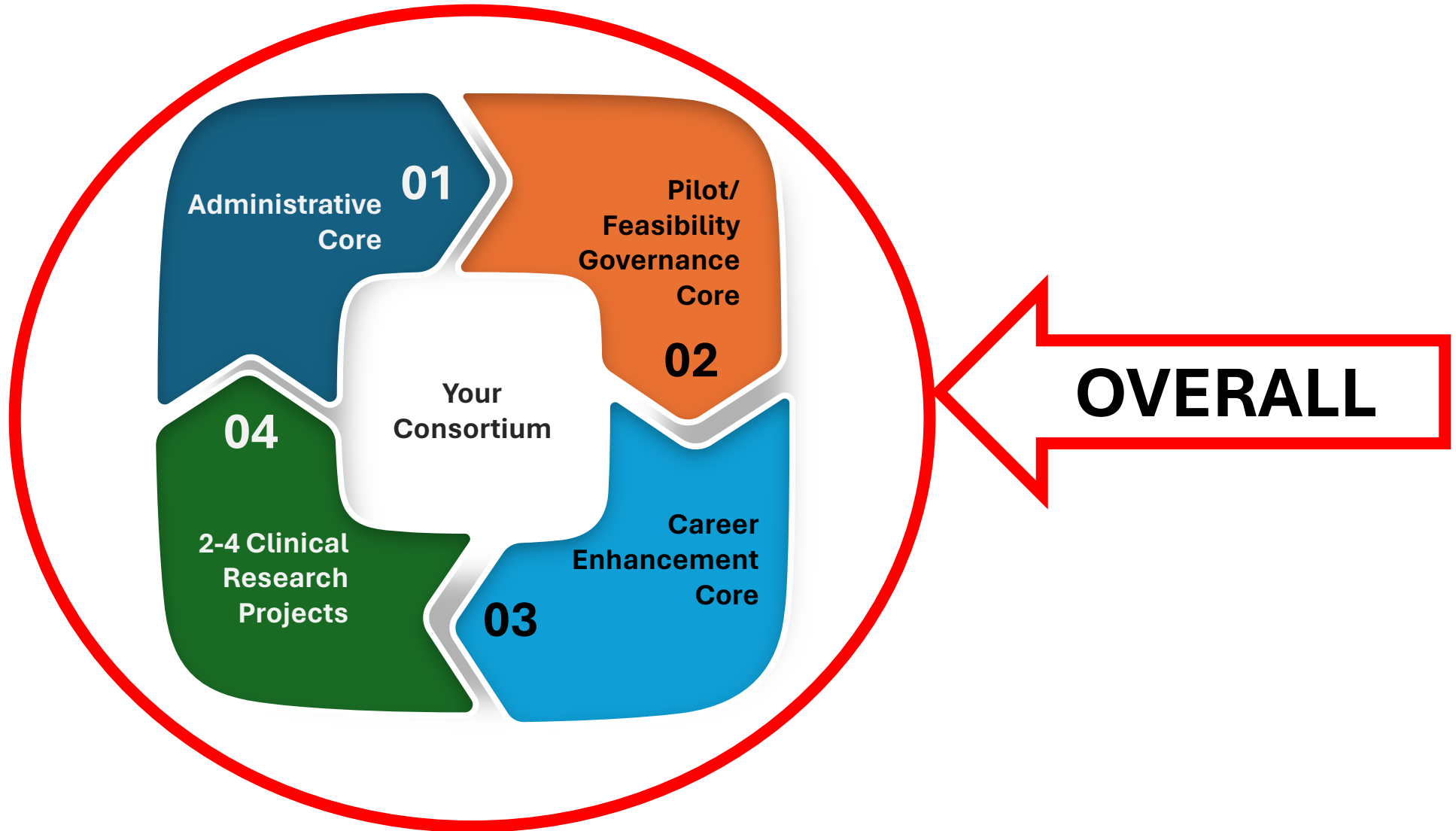
Cores and Projects

Components of an RDCRC

Overall

- Each RDCRC must address specific unmet clinical research needs that will move the field of research forward from its current state of knowledge.
    - This includes activities such as earlier diagnosis of individuals with targeted rare diseases and facilitating more rapid development of new treatments through a program in clinical trial readiness.

- Specific Aims:
    - Describe the overall goals of the RDCRC for the performance period of the grant.
    - Describe the research objectives of the RDCRC for promoting understanding of rare diseases, facilitating early and timely diagnosis and establishing clinical trial readiness.

- Research Strategy:
    - 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.

Administrative Core

- The Administrative Core of each RDCRC will be responsible for the following activities:
  - Administrative Support for RDCRC
  - Management of RDCRC Agreements and Regulatory and Clinical Documentation
  - Coordination of Activities with DMCC
  - Management and Sharing of Data and Biospecimens
  - Collaborating with the DMCC in the Engagement and Dissemination of Information
  - Coordination of Patient Advocacy Groups Participation

Administrative Core Personnel

- **Principal Investigator** - An individual with demonstrated experience in the management of multisite clinical research programs, along with rare disease research should be identified as PI for the Administrative Core.

- **Administrative Coordinator** – An individual with appropriate skills and experience to assist the RDCRC PD/PI and Administrative Core PI with the day-to-day administrative details and program coordination.

- Identified statistical and bioinformatics team members to work collaboratively with the DMCC
    - **Biostatistician** - Individuals with demonstrated strong statistical experience working with rare diseases research as well as clinical trial design and implementation.
    - **Bioinformatics** - Individuals with demonstrated skills in managing RDCRN established data standards, FAIR data principles, and biological data, especially when the data sets are small and complex.

Administrative Support for RDCRC

- Responsible for the overall management of day-to-day program activities for the RDCRC.

- Clear policies and procedures should be established for the RDCRC that dovetail with those of the RDCRN.

- Responsible for coordinating patient advocacy group involvement across RDCRC activities.

- Serves as the primary touchpoint for coordinating collaborations with the DMCC.

Management of RDCRC Agreements and Regulatory and Clinical Documentation

- The Administrative Core will coordinate and manage RDCRC agreements that regulate RDCRC activities.

- The Administrative Core will coordinate and manage all regulatory and clinical documents in collaboration with the NIH and the DMCC (e.g., Investigational New Drug Application (IND), Institutional Review Board (IRB), clinical protocols, consent forms). The Administrative Core will be responsible for coordinating the required single IRB.

Point of Contact with DMCC

- It is important that the RDCRC is prepared to identify a point of contact for communications with DMCC.

- *The RDCRC must not replicate services provided by the DMCC*

Management and Sharing of Data and Biospecimens

- The Administrative Core will coordinate data sharing and biospecimen sharing, storage and tracking information across all clinical sites within the RDCRC and externally with appropriate agreements.

- The DMCC will provide resources for tracking specimens and, via a "virtual repository," indexing biospecimens.

Engagement and Dissemination of Information

- Outreach beyond academic activities is expected; this may include, but is not limited to, dissemination through social media, information and education for the patient community, and collaboration with the patient advocacy group(s) and the DMCC.

- The RDCRC will collaborate with the DMCC to create and manage a RDCRC-specific website.

Pilot/Feasibility Governance Core

- Purpose
  - Enable future pilot studies
  - Advance the diagnosis, clinical trial readiness, management and or treatment of rare diseases
- May be single- or multi-site projects.
- May be awarded to institutions that are not already RDCRC members (may require subaward).
- Specific pilot/feasibility projects must not be described.
- A plan for how pilots will be selected and how results will be disseminated must be included.
- Pilot projects may be clinical trials only with prior NIH institute approval – policies may vary by institute.
- The selection and initiation of pilot/feasibility projects are contingent upon approval by the administering NIH institute and are subject to NIH clinical research regulations.

Career Enhancement Core

- Purpose
  - Play a leadership role in career enhancement
  - Attract new researchers to the rare disease research field
  - Foster diversity, equity, inclusivity and accessibility to research
  - Contribute to the development of future research leaders

- Examples of Career Enhancement candidates include, but are not limited to, the following:
  - Doctoral/Medical students
  - Postdoctoral fellow/researchers
  - Clinical fellows
  - Early-stage investigators
  - Investigators new to the rare disease field

- Leveraging existing programs and exploring fellowship opportunities from other public and private funding organizations is encouraged.

- Propose projects that expand the career enhancement environment.

- Exposure to research at other RDCRCs is encouraged.

Clinical Research Projects

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

- One of the projects must be **longitudinal in nature** with the intent of understanding the clinical course of the disease and helping Inform future clinical trials (e.g., natural history studies).

- Each of the proposed clinical research projects should address problems that **require a substantial collaborative research effort as well as a multi-site RDCRC environment** to solve and can benefit from NIH programmatic input.

- The research projects should be **more substantial than what can be accomplished in a single site project**.

Clinical Research Projects - Clinical Trials

- Any clinical trials proposed as part of a RDCRC must meet ICO-specific rules for clinical trials. **Consultation with relevant ICO contact prior to proposing a clinical trial is highly encouraged.**

- Such clinical trials should be designed to provide specific data that will be necessary to design a subsequent definitive efficacy trial.

- The proposed clinical trial must address questions that, when answered, will optimize the design of a subsequent definitive clinical trial rather than simply address the clinical question with lower power.

Data Management and Coordinating Center

RDCRN Data Management and Coordinating Center (DMCC)

- Overall, the goal of the DMCC is to provide support to each individual RDCRC, and to coordinate and support the activities of the RDCRN as a whole.

- The DMCC will support the consortia by maintaining a robust secure data infrastructure for the RDCRN.

- DMCC Cores include:
  - Administrative Core to facilitate network operation, governance, and communication.
  - Data Management Core to build and maintain a robust, secure data infrastructure.
  - Clinical Research Core to provide guidance in developing best practices in clinical research, protocol development and good data practices using the FAIR principles.
  - Engagement and Dissemination Core to promote patient engagement and broad research dissemination.

RDCRC & DMCC

- It is imperative that RDCRC applicants carefully review the DMCC NOFO to fully understand the resources and services that will be provided to the network participants by the DMCC.

  - RDCRC participants are required to work collaboratively within the RDCRN DMCC cloud environment and to ultimately share their data within RDCRN Data Repository (RDCRN-DR).

  - The RDCRC must not replicate services provided by the DMCC.

  - The RDCRCs will collaborate with the DMCC to establish and promulgate coordinated RDCRN data management and data sharing standards and policies within the RDCRC.

RDCRN Cloud-Based Working Environment

- The DMCC will provide:
  - 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.
  - A management system that provides a "virtual repository" that indexes existing biosamples and other resources within the network.
  - A portal and tools establishing a "tool garden" of shared research tools for research scientists and clinicians to access and manage their own data.
  - Tools provided by NCATS include, but are not limited to, Amazon Web Services, Atlassian, CODECOV, Facebook, Github, MAILCHIMP, Pantheon, Shippo, SHUTTERSTOCK, TWILIO, VIMEO PRO, Seven Bridges, Box.com.

Data Management Services

- The investigative team of the DMCC Data Management Core will manage and facilitate use of Cloud Computing Services and Engineering Support provisioned by the ITRB, NCATS.

- The DMCC will provide RDCRCs access to the cloud instance through the NCATS' Federated Authorization Services and will have complete rights to all services provided by the Cloud Service Provider.

- The DMCC will coordinate and support efforts, in collaboration with representatives of the RDCRC, to develop and monitor Good Data Practices (GDP) of clinical and research data and will assist in facilitating the use of the FAIR principles for data management.

- The DMCC will also facilitate and coordinate data standards across the network.

Data Sharing Environment

- The RDCRN-DR will serve as the central repository for RDCRN-generated clinical research data.

- It will host consented research data from RDCRC-initiated natural history studies, interventional studies and trials, patient reported outcomes and other modalities that were obtained under RDCRN protocols.

- The RDCRN-DR will also function as a central indexing site for RDCRN data that may be required to reside in other NIH-based data repositories, such as the database of Genotypes and Phenotypes (dbGaP https://www.ncbi.nlm.nih.gov/gap/), National Database for Autism Research (NDAR https://nda.nih.gov/).

Institute Specific Research Interests and Priorities

- Prospective applicants are urged to consult with the Scientific/Research Contacts of the NIH early in the preparation of the application.

Scientific/Research Contacts

- **Tiina K. Urv (NCATS)**
  - Telephone: 301-827-2746
  - Email: urvtiin@mail.nih.gov
- **Jill A. Morris (NINDS)**
  - Telephone: 301-496-5745
  - Email: jill.morris@nih.gov
- **Marilyn Miller (NIA)**
  - Telephone: 301-496-9350
  - Email: millerm@nia.nih.gov
- **Melissa Parisi (NICHD)**
  - Telephone: 301-435-6880
  - Email: parisima@mail.nih.gov
- **Marrah Lachowicz-Scroggins (NHLBI)**
  - Telephone: 301-827-8229
  - Email: marrah.lachowicz-scroggins@nih.gov
- **Faye H Chen (NIAMS)**
  - Telephone: 301-594-5055
  - Email: chenf1@mail.nih.gov

- **Zubaida Saifudeen (NIDCR)**
  - Telephone: 301-827-3029
  - Email: zubaida.saifudeen@nih.gov
- **Ruth Florese (NIAID)**
  - Telephone: 301-761-6284
  - Email: ruth.florese@niaid.nih.gov
- **Cindy Roy (NIDDK)**
  - Telephone: 301-594-8805
  - Email: cindy.roy@nih.gov
- **Rongling Li (NHGRI)**
  - Telephone: 301-480-2487
  - Email: lir2@mail.nih.gov
- **Holly Lynn Storkel (NIDCD)**
  - Telephone: 301-451-6842
  - Email: holly.storkel@nih.gov

Scientific Peer Review of the RDCRC

Marilyn Moore-Hoon

Chief, Scientific Review Branch, NCATS

SRB RDCRC Review Team

Lourdes Ponce, SRO

Ming Yan, SRO

Florence Hoffmann, SRO*c

Raymond Schleef, SRO*c

Jeanette Johnson, SRO*c

Rani Khan, Contracts Lead, SRO

Jori Contee-Staten, ESA

Devona Perrineau, Review Specialist

Victor Henriquez, Deputy Chief

Marilyn Moore-Hoon, Chief

Scientific Review Officer = SRO
Extramural Support Assistant = ESA
*c = contactor

Preparing your Application for Submission - Requirements

Required Components

Overall: required

Administrative Core: required; 1 maximum

Pilot/Feasibility Governance Core: required; 1 maximum

Career Enhancement Core: required; 1 maximum

Clinical Research Projects: required; 2 minimum, 4 maximum

Preparing your Application for Submission - Review

Section V. Application Review Information

Reviewer guidance will be based only on the language in Section V

Overall →   Overall Impact
Scored Criteria: Significance, Investigator, Innovation, Approach, Environment

Cores→   Administrative Core

Pilot Feasibility and Career Enhancement Cores

Acceptable, Acceptable with Concerns, or Unacceptable

Projects→   Project

Scored Criteria: Significance, Investigator, Innovation, Approach, Environment

Letter of Intent

Letter of Intent Due Date: JULY 13, 2024

Include the following information:

- Descriptive title of proposed activity
- Name(s), address(es), and telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating institution(s)
- Number and title of this funding opportunity

https://grants.nih.gov/grants/how-to-apply-application-guide/forms-h/multi-project-forms-h.pdf page: m-107

- The letter of intent should be sent to: NCATS Letters of Intent
  - **Telephone: 301-827-9549**
  - **Email: ncatslettersofintent@mail.nih.gov**

Locus of Review and Assignment Request Form

Applications reviewed in a Special Emphasis Panel (SEP) convened by NCATS

Assignment Request Form

- Allows you to indicate your preference for IC assignment for managing the grant/award.
- You may *not* request a Study Section as the locus of review is predetermined.
- You may identify scientific areas of expertise needed to review your application.

Receipt of Applications

DUE Date August 13, 2024
due by 5:00 PM local time of applicant organization.

Submit Early!
Will give time to correct Errors!

Applications have to get through Grants.gov and through the NIH CSR Division of Receipt and Referral – can take up to 2 weeks to get to us!

https://www.grants.gov/applicants/applicant-faqs.htm

https://grants.nih.gov/grants/how-to-apply-application-guide/submission-process/changed-corrected-application.htm l

Application Pre-Review

Administrative Review Completeness/Compliance/Responsiveness

Based on what is in the NOFO

- **Completeness** – anything missing (e.g., no Rare Disease Justification)

- **Compliance** – failed to follow instructions, ineligible

- **Responsiveness** – outside of science/scope/goals

  (e.g., rare disease proposed not in alignment with The Rare Diseases Act of 2002)

The Rare Diseases Act of 2002 (Public Law 107-280 (https://www.govinfo.gov/app/details/PLAW-107publ280))

Determination of Involved Personnel

Review Staff will extract a list of all Involved Personnel and Institutions:
- Includes those listed in the application/biosketches, as well as collaborators, individuals who provided letters of support, advisory board members, and consultants (not always listed on application)

Every Letter of Support and Advisory Member role will be assessed

- Used for determining Conflicts of Interest
- Institutional conflicts are noted for collaborating or participating institutions
- Helpful to have an index of Letters of Support and their authors!

Reviewer Recruitment: Subject Matter Expertise

Focus on stated Rare Diseases, approaches, and structure

- for Overall Application Review

- for each Project

- for Cores

Clear information in your application is vital for reviewers and review staff to understand the science.

Reviewer Recruitment: Other Considerations

- Conflicts of Interest

- Balancing the Roster – diverse panels

- Reviewers Seniority

- Scientific Perspective

- Prior peer review experience

- Breadth of research in the field

- Last-minute emergencies or last-minute COI

Reviewer Training and Guidance

- Webinar training for reviewers covering goals of NOFO and NOFO-specific review criteria and considerations

- Chair and Co-Chair-specific materials

- Meeting materials
  - Reviewer Guidance specific to the RDCRC NOFO
  - Specific RDCRC NOFO tailored review critique templates

Application Review

RDCRC Clinical Research Projects   1-9 Scoring

To what extent…

Significance - Standard NIH Review Criteria *plus*

- …does the research project target gaps to be filled for advancing early diagnosis and treatments for the targeted rare disease/disorder/syndrome/condition?

Investigators - Standard NIH review Criteria *plus*

- …does the investigative team at each clinical site have appropriate experience in the field of rare disease research and expertise required to conduct the proposed research?

Innovation - Standard NIH Review Criteria

RDCRC Clinical Research Projects cont.

To what extent…

Approach - Standard NIH Review Criteria *plus*

- …are the approaches proposed appropriate for rare diseases research?
- …is the study design(s) appropriate for rare diseases research?
- If applicable, … are plans for statistical analysis appropriate for rare diseases research?

Environment - Standard NIH review Criteria *plus*

- …is the environment for the project conducive to completing the project in terms of access to the populations?

To what extent…

Significance

- …will the Administrative Core promote strategies to ensure robust and impactful scientific outcomes for the RDCRC?

Team

- … do the skills and experience of the Administrative Core PI provide the needed knowledge and experience to facilitate the requirements of the Administrative Core?

- …do the skills and experience of the proposed Administrative Coordinator provide them with the ability to assist the RDCRC PD(s)/PI(s) and the Administrative Core PI with day-to-day administrative details and program coordination?

- …does the leadership experience and expertise provide the Administrative Core with the management and coordination skills needed for success for a large RDCRC?

- …is there sufficient collaboration between the bioinformatics and statistical staff, and the DMCC, to ensure appropriate access to the DMCC resources described?

- …is there appropriate effort and expertise for the Administrative Core team to support the RDCRC, including statistical and informatics expertise in rare disease research?

Administrative Core Review (2 of 3)

To what extent…

Communication

- …is there an appropriate plan for promoting awareness of disorders within the RDCRC to the scientific, clinical, and patient/stakeholder communities?
- …will there be coordination with the DMCC for coordinating outreach and communication?
- How effectively will the communication plan ensure participation and coordination between the collaborating investigators, institutions, patient advocacy group(s) and the DMCC?

Approach

- …does the Administrative Core make adequate provisions to meet the needs of the RDCRC and to work collaboratively with the RDCRN DMCC?
- …will the plans for organizational and administrative management lead to success in accomplishing the objectives of the RDCRC? Consider:
  - The management of day-to-day activities.
  - Establishing policies and procedures that dovetail with those of the RDCRN.
  - Funds allocation and establishing contracts with all participating RDCRC sites.
  - Monitoring progress of RDCRC program milestones.

Administrative Core Review (3 of 3)

Approach, cont.

- Considering both RDCRC activities and RDCRN activities, to what extent is the collaboration with the DMCC Cores sufficient to integrate the RDCRC into the network?
- …will the Administrative Core collaborate with the DMCC on the management and coordination of regulatory and clinical documents? Is the proposed timeline for having all agreements with all RDCRC clinical sites in place acceptable and timely? Is there an appropriate timeline for having data use and data sharing agreements in place with the DMCC and is the plan acceptable and timely? Are there appropriate plans for monitoring the quality of ongoing research?
- …will the Administrative Core collaborate with the DMCC to develop and utilize clinical trial readiness metrics for both regulatory requirements and clinical research components to evaluate their progress in clinical trial readiness?
- …will the Administrative Core collaborate with the DMCC to:
  - Facilitate an environment that provides equitable access to information and resources to all participants?
  - Promulgate data management and sharing standards and policies across the RDCRC?
  - Include the use of RDCRN standardized data sharing and data use agreements?
  - Index biosamples and other resources within the RDCRC in a "virtual repository" management system?
- …is the institutional environment, including institutional support, appropriate?

Pilot/Feasibility Governance Core
Rating: acceptable, acceptable with concerns, or unacceptable

To what extent:

- …is the strategy for soliciting and selecting pilot/feasibility projects clearly described? How will the applicant ensure that the solicitation, review, and selection processes are rigorous and unbiased?

- …does the application adequately describe the plan for ensuring that the proposed projects have scientific merit, relationship to the overall goals and activities of the RDCRC, potential to advance the field of research, leverage of existing resources and infrastructure, address diversity and the selection process?

- …does the application adequately address how recipients will award and oversee pilot/feasibility projects, including how they will ensure that NIH prior approval requirements are met, how new subawards will be issued if needed, how awards will be reported to the DMCC, and how the progress of projects will be evaluated for a second year of funding (if applicable)?

- …is the institutional environment, including institutional support, appropriate?

Career Enhancement Core Review
Rating: acceptable, acceptable with concerns, or unacceptable

To what extent:

- …is the Career Enhancement Program administration, including the qualifications of the core leader and the proposed oversight and monitoring, appropriate?
- …are the proposed faculty appropriate for the Career Enhancement candidate(s) and do they have a strong record of research and mentoring?
- …are the proposed career enhancement activities, including those unique to clinical research with rare diseases and those focused on workforce development appropriate?
- …if strategies are proposed to promote fellowship funding from other public/provide funding organizations, are the plans for facilitating grant writing, refining applications tracking, and reporting on fellowship success well considered and described?
- If direct support for Career Enhancement candidate(s) is proposed, …is the nomination and selection process appropriate for the proposed Career Enhancement Program?
- …is the institutional environment, including the institutional support and the proposed interaction with existing Career Enhancement Programs, appropriate?
- …is the plan to review and determine the quality and effectiveness of the Career Enhancement Program adequate?

- For renewal applications, …has the program been successful in meeting the goals of the Career Enhancement Program?

Overall Review (1 of 3)
Criteria Scoring 1-9, Overall Scoring 1-9

To what extent…

Significance - Standard NIH Review Criteria *plus*

- …is there sufficient rationale provided for the rare diseases chosen? **Consider whether these rare diseases can be reasonably grouped together to move the individual fields forward.**

- …do the clinical projects and cores demonstrate a focus on unmet research/clinical needs for the targeted rare diseases?

- …will the proposed RDCRC accelerate progress toward effective treatments or other improvements in the lives of individuals with the targeted rare diseases through coordinated and collaborative research and infrastructure activities?

- …**are the clinical projects and cores individually meritorious and complementary to the overarching goals of the RDCRN? If successful, how might the proposed RDCRN advance understanding of the diseases, facilitating early diagnosis, improving clinical trial readiness, developing and testing therapies, advancing patient care and reducing disease burden?**

- …is there sufficient justification for the need for the RDCRN center infrastructure over completing the research via traditional grant mechanisms?

Criteria Scoring 1-9, Overall Scoring 1-9

To what extent…

Investigator - Standard NIH Review Criteria *plus*

- To what extent is the PD(s)/PI(s) rare disease expertise and experience appropriate for managing large multi-component clinical research programs in rare diseases addressed?

Innovation - Standard NIH Review Criteria

Environment - Standard NIH Review Criteria *plus*

- …is the rationale for choosing clinical sites adequate and justified? To what extent does the overall RDCRC include a diverse set of sites?
- …is the institutional commitment appropriate for supporting a rare diseases research center?

Criteria Scoring 1-9, Overall Scoring 1-9

To what extent…

Approach - Standard NIH Review Criteria *plus*

- …are patient and stakeholder experiences, needs and priorities meaningfully incorporated as partners into decisions and activities of the RDCRC?
- …are the plans to work with the DMCC and leverage the shared network tools provided by the NIH appropriate?
- …are the plans for the RDCRC to collaborate and otherwise contribute to the RDCRN meaningful?
- …are the plans adequate to ensure and maintain collaborative relationships across multiple research sites and the RDCRC?

Timeline for Review

- Applications will only be assessed using language from the RDCRC NOFO Section V!

- Review of multiple LARGE applications takes time

- **Special Emphasis Panel review meeting planned for Jan/Feb 2025**

- Summary Statements for large applications take time but will be released no later than April 20, 2025

Post Meeting

- Check your Official Grant Folder for your Summary Statement
    - Summary Statements will be released no later than April 20, 2024
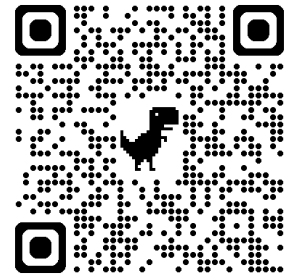   - Please wait until your SS is released to contact your PO

THANK YOU !

Post Webinar Information

- If you have general questions after the webinar, please submit them to:
  - NCATS_RDCRN@mail.nih.gov

- Answers to questions not addressed during the webinar will be provided on the NCATS RDCRN Applicant Information page:
  - https://ncats.nih.gov/research/research-activities/RDCRN/applicant-information

- Questions that are specific to your application/science will not be answered during the webinar. Please reach out to the appropriate NIH PO.

- Sign language interpreting and real-time captioning services are available upon request for the June 3rd session of this webinar.

- Individuals requiring either of these services and/or other reasonable accommodation, please contact Chris Maurer at christopher.maurer2@nih.gov or 301-827-7280 by Friday, May 24.

Thanks to our great team members who have made this webinar possible

- Joanne Lumsden
- PJ Torres
- Ainslie Tisdale
- Meera Shah

Questions and Answers

Send your questions to:

NCATS_RDCRN@mail.nih.gov