

Rare Diseases Clinical Research Consortia (RDCRC) for RDCRN: Pre-Application meeting

Preparing to submit a U54 Application for RDCRC (RFA-TR-13-002)

Wednesday, September 25th, 2013

1:00 PM EST

6001 Executive Blvd. Rockville, Maryland

Meeting Agenda

Introduction (*Dr. Stephen C. Groft*)

Office of Rare Diseases Research, NCATS

Overview of RDCRC RFA

RDCRC RFA (*Dr. Rashmi Gopal-Srivastava*),

Office of Rare Diseases Research, NCATS

Q & A Session

Answer Questions Related to Submission of Application

- Live audience: use microphone
- Video-Cast Audience: send email to
“Live Event Feedback Form” (ordr@mail.nih.gov)

Slides will be posted: <http://videocast.nih.gov> and
<http://rarediseasesinfo.nih.gov>

INTRODUCTORY REMARKS

DR. STEPHEN C GROFT
DIRECTOR, ORDR/NCATS

NCATS

Historical Goals of RDCRN

- **Rare Diseases Act Of 2002 Mandated The Development Of Centers Of Excellence For Rare Diseases**
- **Demonstrate The Ability To Conduct Clinical Studies And Clinical Trials of Rare Diseases With Small Patient Populations Under A Common Protocol**
- **Demonstrate The Value And Need For Longitudinal And Natural History Studies**

Historical Goals of RDCRN (Continued)

- **Develop An Expanded Role For Patients And Patient Advocacy Groups With Recognition Of Need To Establish Collaborative Partnerships**
- **Develop Collaborative Partnerships With Industry, Other Academic And Government Investigators And Institutions**
- **Establish A Critical Mass Of Investigators And Available Patients To Open And Complete Clinical Studies In A Timely Fashion Without Extraordinary Delays**

Results of First 10 Years of RDCRN Activities

- Time Required To Open Studies To Patient Recruitment Has Been Reduced
- Patient Recruitment Into Studies Has Been Facilitated By...
 - Use Of The Contact Registry
 - Expanded Role of 95 Patient Advocacy Groups And
 - Presence on the Internet
- Increased Number Of Consortia From Four To 17
- Increased NIH Institute And Center Involvement To 10
- Clinical Trials To Meet Regulatory Requirements Of New Drug Applications Are Possible And Encouraged In RDCRN Consortia

Pre-Application meeting: Rare Diseases Clinical Research Consortia (RDCRC) for Rare Diseases Clinical Research Network:

RASHMI GOPAL-SRIVASTAVA, PH.D.
DIRECTOR, EXTRAMURAL RESEARCH PROGRAM
OFFICE OF RARE DISEASES RESEARCH, NCATS
SEPTEMBER 25TH, 2013

NCATS

RDCRN: Goal

The Rare Diseases Clinical Research Network (RDCRN) should facilitate

- Identification of biomarkers for disease risk, disease severity/activity
- Identification of measures of clinical outcomes appropriate for applicability to clinical trials
- Encourage development of new approaches to diagnosis, prevention, and treatment of rare diseases

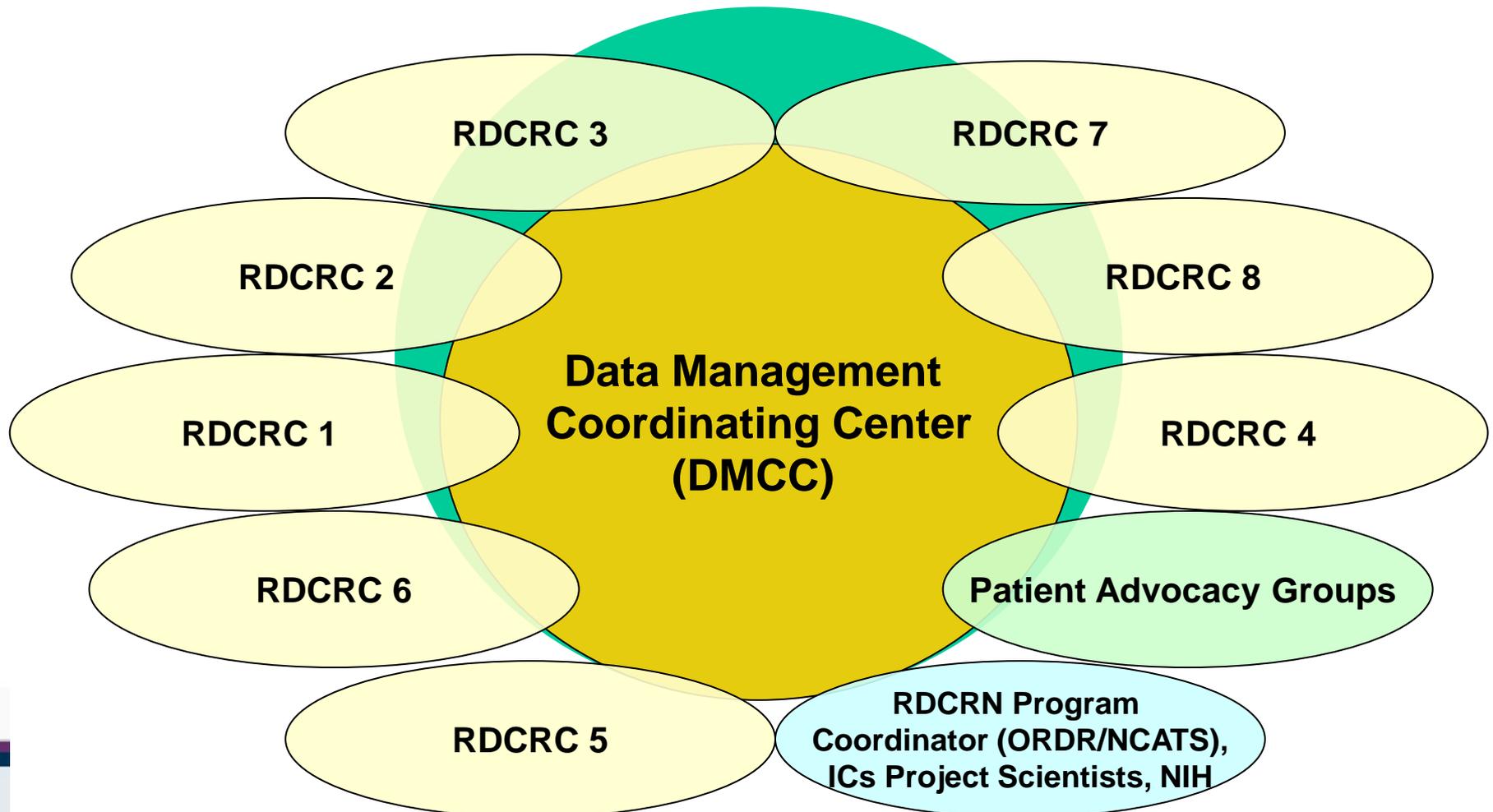
Rare Disease Clinical Research Network (RDCRN)

- **Reissuance of RDCRC RFA**
- **RDCRC RFA Partners**
NCI, NHLBI, NIAID, NIAMS, NICHD, NIDCR, NIDDK, NINDS, * NEI, * ODS

*New partners
- **RDCRN (RDCRCs and DMCC).** (two components of the same program)

RDCRN Structure

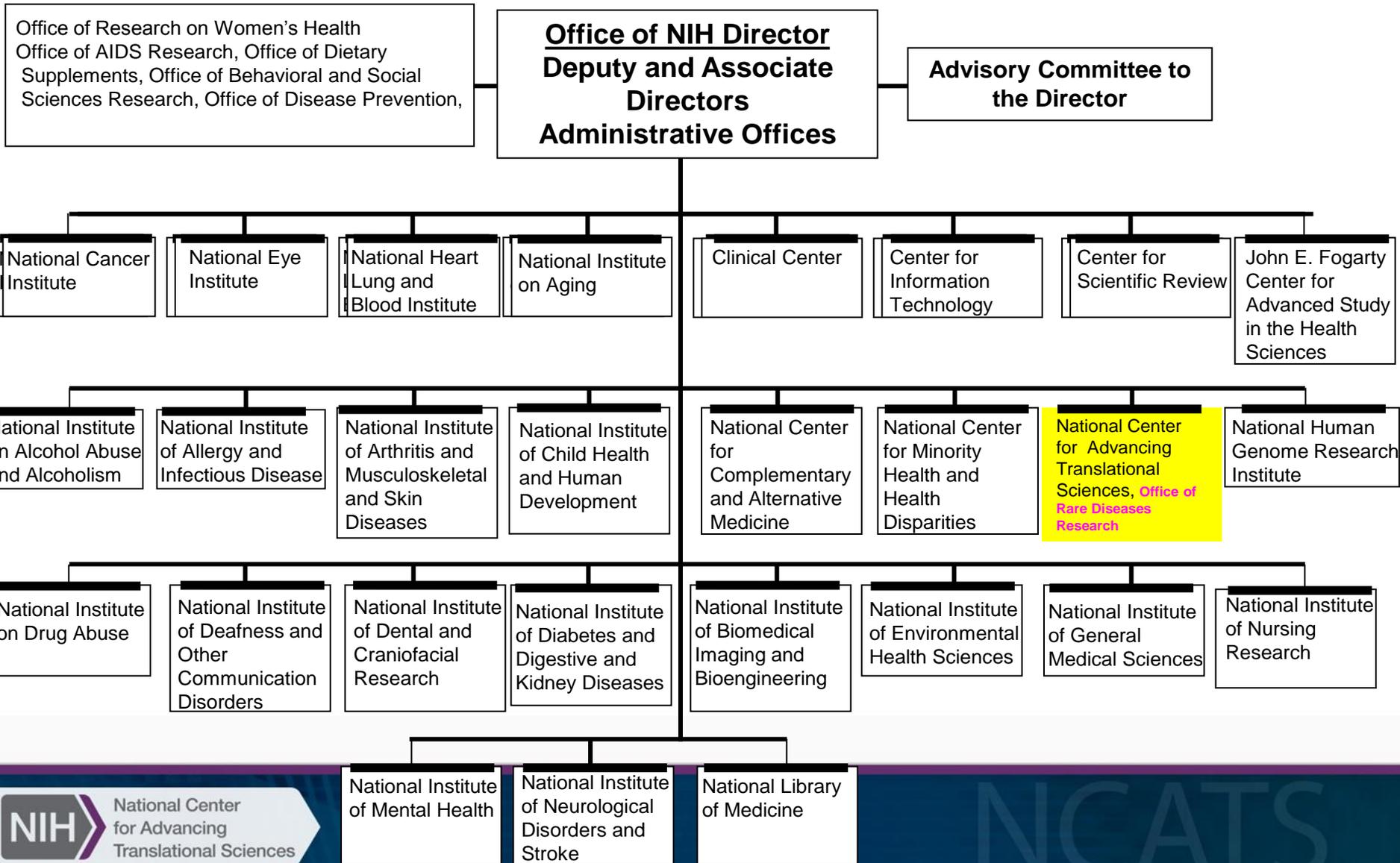
Rare Diseases Clinical Research Network



Rare Diseases Clinical Research Consortia (RDCRC)

RFA-TR-13-002 (U54)

The View of the NIH

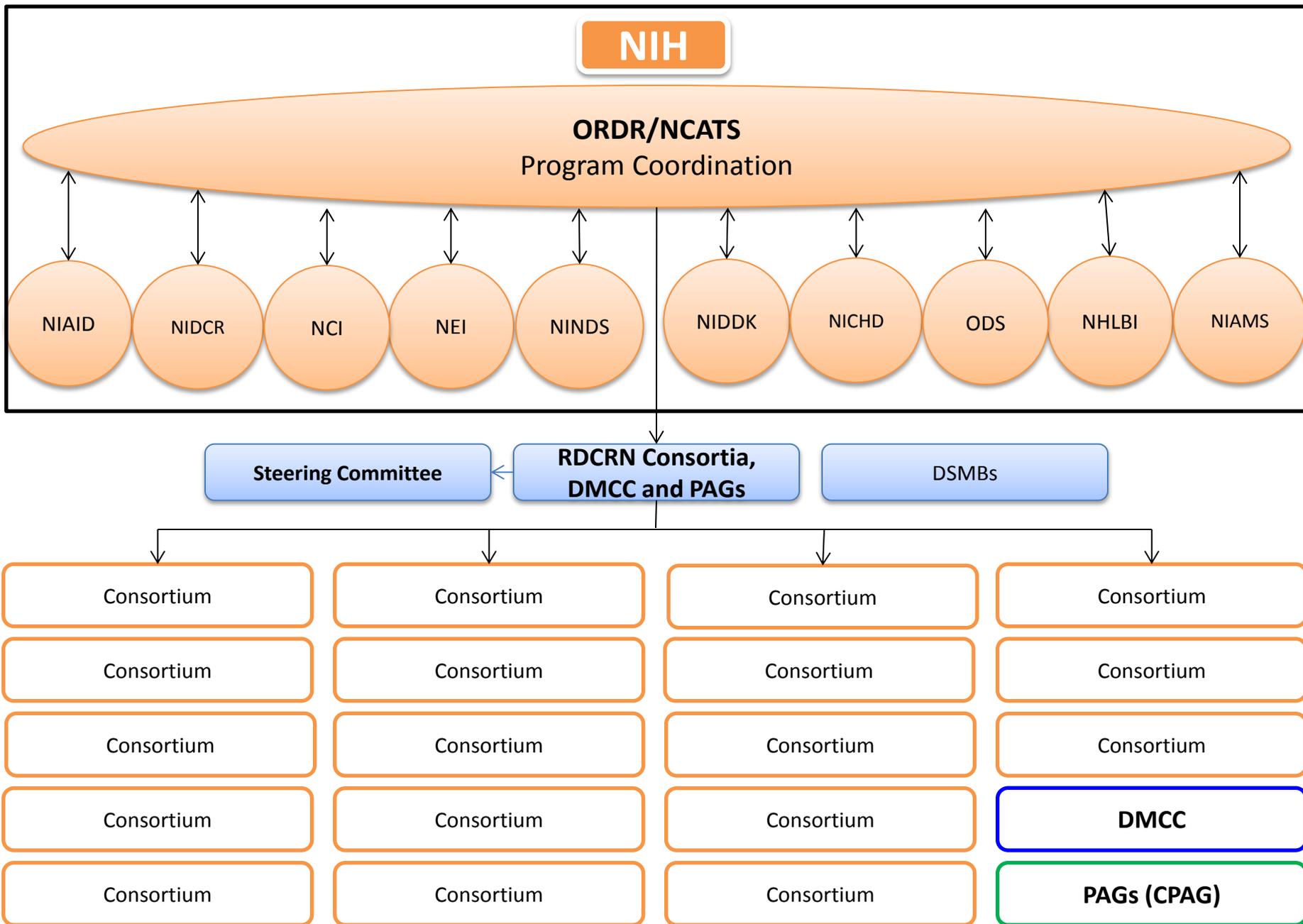


Organization & Management of RDCRN

- The Rare Diseases Clinical Research Network (RDCRN) will consist of all funded Rare Diseases Research Consortia (RDCRC) and a single Data Management and Coordinating Center (DMCC).
- Support by cooperative agreement mechanism

Note: DMCC RFA for RDCRN (will be published separately)

Rare Disease Clinical Research Network (RDCRN)



RDCRC RFA: IC Program Contact

ORDR/NCATS: Rashmi Gopal-Srivastava, Ph.D. (Program Coordinator for RDCRN Cooperative Agreement Program)

- NCI: Elizabeth Read-Connole, Ph.D.
- NEI: Grace L Shen, Ph.D.
- NHLBI: 1) For rare heart diseases: Michelle Olive, Ph.D.,
2) For rare lung diseases: Susan Banks-Schlegel, Ph.D.
3) For rare blood diseases: Andrei L. Kindzelski, M.D., Ph.D.
- NIAID: Linda M. Griffith, M.D., Ph.D.
- NIAMS: James Witter MD, Ph.D
- NICHD: Mary Lou Oster-Granite, Ph. D.
- NIDCR: Jane Atkinson, D.D.S.
- NIDDK: Ellen Lescheck, M.D.
- NINDS: 1) Laura A. Mamounas, Ph.D.
2) Randall R. Stewart, Ph.D.
- ODS: Kathryn Camp, M.S, R.D., CSP

Note: Also see Financial/Grants Management contacts and **“IC-Specific Research Area of Interest”**

Meeting Agenda: RDCRC RFA

Overview



- Time Lines
- RFA Purpose
- Requirements
- Review of Applications
- Reminders

Your Questions?

Timeline for RFA-TR-13-002

- **Letter of Intent (optional)** **October 7th, 2013**
- **Application Receipt** **November 7, 2013**
- **Peer Review** **January-February, 2014**
- **Council Review** **May, 2014**
- **Earliest Anticipated Award Date** **July, 2014**

RDCRC Letter of Intent: Content

- **Draft Consortia (RDCRC) Title**
- **RFA ID: TR-13-002, Rare Diseases Clinical Research Consortia for RDCRN**
- **Principal Investigator, with contact info**
- **Other Key Personnel**
- **Participating Institutions**
- **(Optional: Brief description of projects)**

Submit to: Dr. Rashmi Gopal-Srivastava
(gopalr@mail.nih.gov)

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Your Questions?

Purpose of RDCRC RFA

The purpose of the RDCRC is to facilitate clinical research in rare diseases through support for:

- collaborative clinical research in rare diseases, including longitudinal studies of individuals with rare diseases, clinical studies and/or phase I , II and II/III trials;
- training of investigators in clinical research of rare diseases;
- pilot/demonstration projects
- access to information related to rare diseases for basic and clinical researchers, academic and practicing physicians, patients, and the lay public. (Website resource for education and research in rare diseases)

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RDCRC: Required Components/Activity

Both New and Renewal applications focused on at least three rare diseases will be accepted.

Required components/activities of an RDCRC (U54) application include

- A minimum of two clinical research projects (at least one of them must be a longitudinal study)
- A Pilot/Demonstration Clinical Research Projects Program
- A training (career development) component
- A website for educational and research resources in rare diseases
- An administrative unit
- Collaboration with patient advocacy group(s)

Each RDCRC Will ...

- Perform collaborative clinical research focused on a group of at least three rare diseases that are relevant to the interests of the participating NIH ICs.
- Consist of a consortium of clinical investigators, multiple institutions, and relevant organizations, including patient advocacy groups as research partners.
- Train new investigators in rare diseases research, and
- Provide content for an internet resource site on rare diseases.

Each RDCRC application must include the following components and activities:

Overall

- RDCRC Program Introduction and Statement of Objectives
- RDCRC Scientific and Administrative Leadership
- Multidisciplinary Team Involving Patient Advocacy Groups and collaborations
- Environment and Website for Education and Research
- Rare Diseases Patient Population
- Institutional Commitment
- Resource Sharing Plan

1) Clinical Research Projects for Observational/Longitudinal Studies or Clinical Trials

(At least two projects are required *and one of them must be a longitudinal study*)

- Describe the rationale for the planned clinical studies and longitudinal assessment of subjects. Strategies for recruitment, retention, assessment, and analysis must be included.
- The clinical studies could include strategies for assessing current therapeutic interventions, and phase I, II or II/III clinical trials.

Note: Clinical trials are not a required component of an RDCRC

Clinical Research Projects: Longitudinal Studies

- Applicants must propose clinical research projects that can characterize and more completely define the disease and its course for the rare diseases. These, in general, will be observational (non-interventional), such as longitudinal or natural history studies of patients with the given disease.
- The study design and objectives should take in to consideration what information regarding the rare disease population would be needed in order to pursue clinical trials for that rare disease.
- Projects for time period of five years.

Clinical Research Projects: Longitudinal Studies (Cont.)

- Applicants should approach a longitudinal study with the question: What knowledge/tools are needed regarding the rare disease in order to design efficient efficacy trials for this rare disease?
- Even if there are no treatments currently proposed for the rare diseases under study, a longitudinal study should be designed with the intention that if a treatment was suddenly available, what knowledge (outcome measures, features of disease course, markers of disease or subpopulations of the rare disease that may alter disease course, etc.) about the rare disease over time would be important to have to design an appropriate treatment (efficacy) trial.

2) Pilot / Demonstration Clinical Research Projects Program

- Propose pilot projects that generate feasibility data and have the most promising clinical research potential.
- To support studies of a limited duration, of 2 years or less.
- Include a plan addressing attracting new ideas and pilot studies and continuously reviewing and funding a spectrum of pilot projects with clinical research potential.
- Include description, examples and provide rationale for the planned pilot projects. Must be maintained throughout the entire term of the cooperative agreement award.
- Examples also include development of novel laboratory assays and clinical instruments, development of tools for drug discovery (e.g. development of bioassays for screening compounds), analysis of extracellular RNAs as biomarkers of disease and/or response to therapeutics, retrospective chart review from different study sites.
- Depending on the state of knowledge of the particular diseases, the pilot studies could include strategies for assessing current therapeutic interventions, phase I, II, or II/III clinical trials.

3) Training (Career Development) Component

- Each application must include a plan for training.
- The RDCRC should provide a unique environment for clinical research that will prepare new scientists for careers in this field.
- A minimum of \$50,000 direct costs per year from the RDCRC budget must be dedicated to this program
- Include criteria and process of selecting candidates.
- Include a short description of types and qualifications of potential candidates, as well as the qualifications and research activities of mentors.

4) Website resource for education and research in rare diseases

- Describe resources to be included in a web site for education and research in rare diseases (should include links or materials for lay public, patients, basic and clinical researchers, and clinicians).
- Examples: contacts for animal models; availability of tissue, serum, specimens, DNA, etc.; antibodies and research reagents; genetic resources; registries; education materials; and/or diagnostic flow charts.
- Each RDCRC and the DMCC must agree to work cooperatively to develop the web site resource and provide content related to the RDCRC's specific rare diseases.

5) RDCRC Administrative Unit

An Administrative Unit is required. It will be responsible for:

- Overall administration of the RDCRC, Coordinating activities for RDCRC, Coordinating Network connections (DMCC, ORDR, NCATS, NIH ICs, PAG)

Describe:

- the chain of responsibility for decision-making and administration.
- a plan for communication (meetings, conference calls, etc.) and participation of all personnel within the consortium.

This unit must include:

- A clinical investigator. Identify an *Administrative Director* on the application who will be responsible for assisting the RDCRC Director (PI of the application)
- Describe the biostatistical support for the RDCRC in this section. The biostatistician will provide statistical support for protocol development and assist in study designs.

6) Collaboration with Patient Advocacy Group (PAG)

- Include a plan to fully incorporate the relevant PAG(s) within RDCRC structure and interactions (conference calls, meetings etc.).
- Describe their participation across the planned objectives (e.g. in addressing clinical design, recruitment and education).
- The proposed activities should be appropriate for the level of the PAG(s).

Renewal Applications: Additional Material Required

- All applications for renewal must provide information documenting the impact of the clinical research from the original application.
- See Section V. Application Review Information for the review criteria to be addressed.

Summary

An RDCRC must include the following:

1. Clinical Research Projects for Observational/Longitudinal Studies and/or Clinical trials (At least two projects are required, one of which must be a longitudinal study)
2. Pilot/Demonstration Projects Program
3. Training (career development) Component
4. Website resource for education and research in rare diseases
5. RDCRC Administrative Unit
6. Collaboration with Patient Advocacy Group and

An Overall Description

Remember ... It is a Network of Consortia

- You will propose the direction and organization of your RDCRC
- Awarded RDCRCs will be formed into a Network (RDCRN) including a DMCC
- Oversight will be from RDCRN Steering Committee (SC)
- All participating PAGs will form Coalition of Patient Advocacy Group (CPAG) for RDCRN.
- Support by cooperative agreement mechanism (\$1.25M Total cost per year)

RDCRN Steering Committee

Purpose

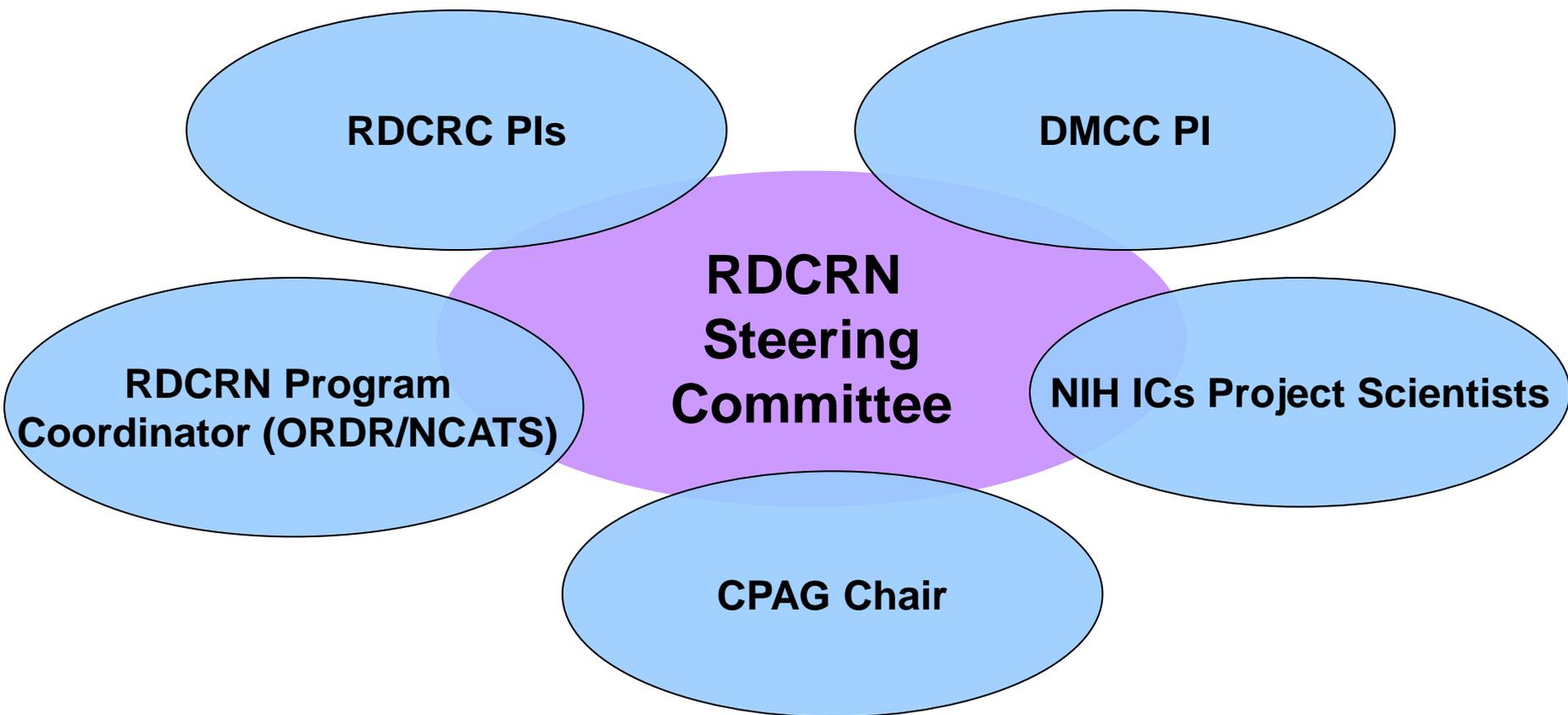
- Review, facilitate and establish all Network procedures and functions through monthly teleconference calls and face to face meetings, schedule & plan agendas

See RFA for details

Organization

- Voting Members: PIs for RDCRC, DMCC PI, RDCRN Program Coordinator from ORDR/NCATS, NIH ICs Project Scientists, and CPAG Chair
- One PI elected as chairperson
- Invitees: Other (non-voting) members, (program officials from IC, and ORDR)

RDCRN Steering Committee Organization



Meeting Agenda: RDCRC RFA

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Your Questions?

Review of Applications

- Special Emphasis Panel (SEP)
- Organized by NCATS-
(Dr. Carol Lambert, Scientific Review Officer)
- Panel will review only responses to this RFA
- Special instructions given to reviewers

The Scientific Peer Review Process

- Will be driven by the number of applications received.
- Will use expedited review process (triage)
- Will generate a summary statement (written critique) for each application

Review Criteria for RDCRC

- Following few slides are just samples of review criteria and do not include ALL review criteria
- See RFA for all review criteria

Review Criteria: Clinical Research Projects

- **Significance**
- **Approach**
- **Innovation**
- **Investigators**
- **Environment**

Review Criteria: Pilot / Demonstration Projects Program

- Does the proposed plan address attracting new ideas and pilot studies within RDCRC institutions?
- Does the plan address continuously reviewing and funding a spectrum of pilot projects with clinical research potential in rare diseases?
- Will the proposed plan support projects that take maximum advantage of new clinical research opportunities in rare diseases?

Review Criteria: Training (Career Development) Component

- Is the plan for training new investigators adequate and appropriate?
- Does the plan describe how promising candidates for clinical research in rare diseases will be selected?
- Are environments within RDCRC appropriate for supporting the training of new investigators of the rare diseases under study?
- Does the proposed plan address how the investigators will seek out and include qualified women and minorities for participation in the proposed program?

For renewal applications: Remember to provide current status and clinical research activities of individuals who have been supported by the training program.

Review Criteria: RDCRC Administrative Unit

- Are the plan(s) for overall administration of RDCRC, coordination of clinical research and collaborations presented and sufficient for the requirements of the proposed RDCRC?
- Is the plan for communication and participation of all personnel within the consortium well described?
- Does the RDCRC provide appropriate biostatistical support?

Review Criteria: Overall

Leadership:

- Are the scientific qualifications and involvement of the PD/PI (RDCRC Director) and Administrative Director as well as his/her scientific and administrative leadership capabilities and time commitment presented and sufficient for the requirements of the proposed RDCRC?

Rare Diseases Patient Population:

- Is the access to rare diseases patients and populations for conducting clinical research adequate to ensure likely success of the goals of the program?

Overall *(continued)*

Institutional Commitment:

- Are there features in the institutional environment that are relevant to the effective implementation of the proposed program?
- Is there institutional commitment to establishing the RDCRC as an integral part of its overall clinical research environment?
- Is there commitment from the institutional leadership to protect the time of the investigators to pursue clinical research and mitigate the demands of providing patient care?
- Will the clinical researcher/trainees be supported for the training program?
- Is the institutional leadership committed to this program and its goals in terms of providing specific assets specifically for the program, such as faculty support, specific equipment, dedicated space, or financial support as a few examples?
- Will the institution align or adjust incentives and rewards to promote the academic mission of collaborative rare diseases research?
- Do the plans for integrating the activities of RDCRC clinical research projects, as well as integrating rare diseases research with existing institutional resources (e.g., use of clinical data and safety management systems, biostatistical support, etc.), give confidence and sufficient evidence that such efforts are likely to be effective?

Overall *(continued)*

Multidisciplinary Team Involving Patient Advocacy Groups (PAG) Collaborations:

- Is there a plan to fully incorporate the relevant PAG within RDCRC structure and interactions (conference calls, meetings etc.)?
- Is PAG participation described across the planned objectives (e.g. in addressing clinical design, recruitment and education)?
- Are proposed activities appropriate for the level of the PAG(s)?
- Is there evidence of tangible interactions with PAG(s)?
- Is there evidence of tangible interactions with participating sites?

Additional Review Criteria

- Protection of Human Subjects
- Inclusion of Women, Minorities and Children
- Biohazards
- Renewals

Review Criteria: Progress for Renewal Applications

- Are the progress and achievements specific to the application and relevant to clinical research since the previous competitive review?
- Has adequate progress been demonstrated on clinical research projects that are ongoing? Are there any difficulties in achieving the previously proposed specific aims addressed?
- Is it evident that the investigative team established a productive working relationship among themselves and with the Patient Advocacy Groups during the past performance period?

Additional Review Considerations

- Resource sharing plans
- Plan for streamlining protocol approval process

Review and Selection

The following will be considered in the selection process (funding decision):

- Scientific merit of the proposed RDCRC as determined by peer review
- Availability of funds
- Relevance to NIH ICs and ORDR/NCATS program priorities

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Your Questions?

Read and Comply with RFA Instructions

- Remember, this is a paper submission.
- Include all required and recommended components.
- Follow the suggestions on page recommendations (limits) for each component.
- Follow the NIH instructions on Appendix materials (consult the URL in the RFA).
- Read Terms and Conditions of Cooperative Agreement.
- Read the review criteria carefully to understand the basis for the evaluation. *For renewal applications:* documentation of accomplished clinical research goals.

Page Limitations

All page limitations described in the PHS 398 Application Guide and the [Table of Page Limits](#) must be followed, in addition to the following page limitations to the *Research Strategy* section of each component of the application.

- Overall: 12 pages
- Clinical Research Projects for Observational/Longitudinal Studies: 12 pages for *each* project
- Pilot/Demonstration Clinical Research Projects Program: 12 pages
- Training (career development) Component: 6 pages
- RDCRC Administrative Unit: 6 pages

Application Preparation

- Read and follow the instructions in PHS 398 (Revised 8/2012) and “Other Submission Requirements”.
- Make sure your application is complete.
- For supplemental material after the receipt date see NOT-OD-13-30 and NOT-OD-10-115.
- If human subjects are involved include a targeted planned enrollment table.
- Don't forget data and safety monitoring requirements
- Have a statistician assess statistical power for all studies

RDCRN (RDCRCs + DMCC)

- The RDCRN will require cooperation among the PIs of the RDCRCs and their collaborators, the PI of the DMCC, RDCRN Program Coordinator from ORDR/NCATS and the participating IC Project Scientists, to maximize their effectiveness.
- A number of issues need to be addressed in the cooperative agreement applications (including those highlighted in Organization of the Rare Diseases Clinical Research Network and under Cooperative Agreement Terms and Conditions.)

Reminder

- **Contact IC Program and GM staff and see “IC Research Areas of Interest”**
- **RDCRC RFA Page**
<http://grants.nih.gov/grants/guide/rfa-files/RFA-TR-13-002.html>
- **RDCRN Program Director: Dr. Rashmi Gopal-Srivastava**
[\(gopalr@mail.nih.gov\)](mailto:gopalr@mail.nih.gov)

Meeting Open for Questions

- **Start with previously received questions for RDCRC**
- **Live questions for RDCRC**

Q & A Session

Answer Questions:

- **Live audience: use microphone**
- **Video-Cast Audience: send email to “Live Event Feedback Form” (ordr@mail.nih.gov)**

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Thank you!

