

Synergizing Epidemiologic Research on Rare Cancers

May 10–11, 2007

Hyatt Regency Hotel, Bethesda, MD

Sponsored by

National Cancer Institute (NCI)

DCCPS/EGRP and

NIH Office of Rare Diseases (ORD)

**Rare Diseases
Clinical Research Network
(RDCRN): A Network of Consortia**

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Office of Rare Diseases (ORD)
National Institutes of Health (NIH)*

Rare Diseases Act of 2002

Public Law 107-280 (November 6, 2002)

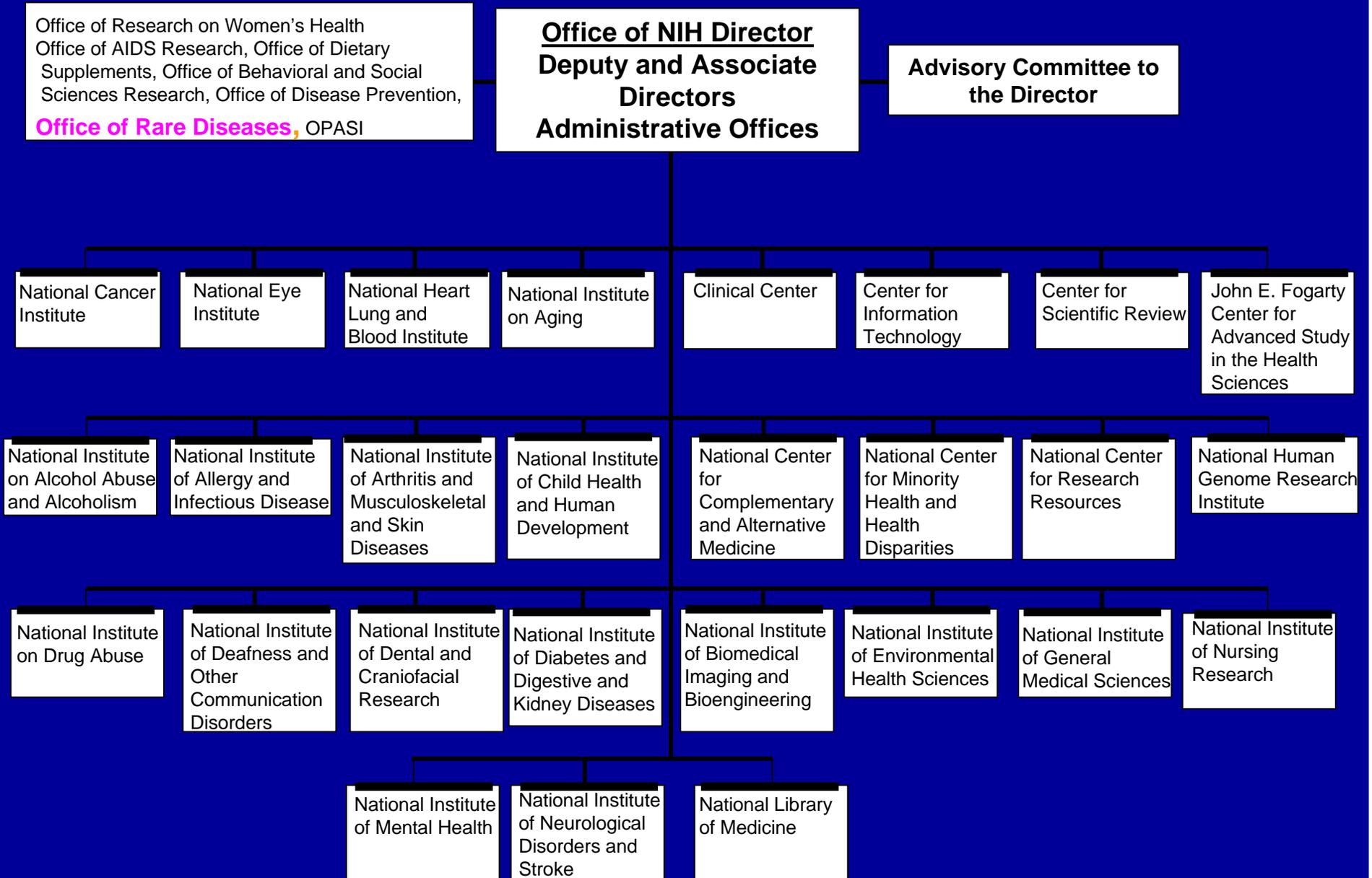
Purposes:

- Amend the Public Health Services Act to establish an Office of Rare Diseases at the NIH and
- Increase the national investment in the development of diagnostics and treatments for patients with rare diseases

Rare Diseases

- **Rare Diseases are diseases or conditions which affect less than 200,000 patients in the USA**
- **or a disease with a greater prevalence but for which no expectation exists that the costs of developing or distributing a drug can be recovered from the sale of the drug in the United States.**

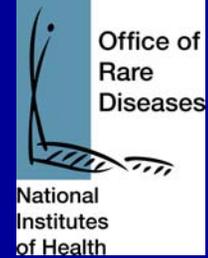
The View of the NIH



The NIH OFFICE OF RARE DISEASES (ORD)

- **Stimulates and coordinates research on rare diseases and**
- **Supports research to respond to the needs of patients, healthcare providers and the research communities involved in the care, treatment, and evaluation of products for the prevention, diagnosis, or treatment of almost 7,000 rare diseases known today.**
- **For more information about ORD and its programs, visit**
<http://www.rarediseases.nih.gov>.

ORD Areas of Strategic Initiatives



- Collaborative Clinical Research Programs
- *Intramural Research Program*
 - Bench to Bedside Program
 - Clinical and Biochemical Genetics Training Program
- *Extramural Research Program*
 - Scientific Conferences
 - Rare Diseases Clinical Research Network (RDCRN)

Background: Rare Diseases

The Problem:

- ~ 25 million people in the United States are affected by one of approximately 6000 rare diseases.
- Patients with rare diseases are frequently misdiagnosed or are undiagnosed.
- Few drug companies conduct research into rare diseases since it is difficult to recoup the costs of developing treatments for such small, geographically dispersed populations.

To advance medical research on rare diseases, a research network would facilitate collaboration, enrollment in studies and trials, and sharing of data.

**Rare Diseases
Clinical Research Network
(RDCRN)
Established by NIH**

RDCRN Background

- Established in 2003 - (in response to RFA)
- Four Rare Disease Consortia → Ten by 2004 (ORD, NCRR, NHLBI, NICHD, NIDDK, NIAMS, NINDS)
- One Data and Technology Coordinating Center (DTCC)
- Each Consortium: multiple diseases
- Consortium of Clinical Investigators, Institutions, Patient Support Groups

Goals of RDCRN

- **Facilitate Collaborative Clinical Research in Rare Diseases**
- **Conduct clinical-translational research on multiple rare diseases including:**
 - Longitudinal studies, Diagnostics, and Therapeutic clinical trials**
- **Develop innovative tools to collect and manage geographically distributed clinical research data using standardized data elements**
- **Provide training in clinical research on rare diseases**
- **Improve (Web) access to information about rare diseases for Clinicians, Researchers, and the Lay Public and**
- **Support demonstration projects**

Configuration of the Network: 10 Rare Disease Consortia

- **Angelman, Rett, & Prader-Willi Syndromes**
ARPWSC Beaudet
- **Bone Marrow Failure Disease** **BMFDC**
Maciejewski
- **Cholestatic Liver Disease** **CLiC** Sokol
- **Clinical Investigations of Neurological
Channelopathies** **CINCH** Griggs
- **Genetic Disorders of Mucociliary Clearance**
GDMCC Knowles

10 Rare Disease Consortia

- Rare Genetic Steroid Diseases **RGSDC** New
- Rare Lung Diseases **RLDC** Trapnell
- Rare Thrombotic Diseases **RTDC** Ortel
- Urea Cycle Disorders **UCDC** Batshaw
- Vasculitis Clinical Research **VCRC** Merkel

- Data and Technology Coordinating Center **DTCC** Krischer
- Steering Committee PIs, NIH, PAG

Bone Marrow Failure Disease Consortium (BMFDC)

- **Aplastic Anemia**
- **Myelodysplastic Syndromes**
- **Large Granular Lymphocyte (LGL) Leukemia**
- **Paroxysmal Nocturnal Hemoglobinuria (PNH)**
- **Single Lineage Cytopenias:**
- **Pure Red Cell Aplasia**
- **Amegakaryocytic Thrombocytopenic Purpura**
- **Autoimmune Neutropenia**

Rare Diseases Under Study

n=45

Alagille Syndrome

Alpha-1 Antitrypsin Deficiency

Amegakaryocytic

Thrombocytopenic Purpura

Andersen-Tawil Syndrome

Androgen Receptor Defects

Angelman's Syndrome

Antiphospholipid Antibody
Syndromes

Aplastic Anemia

Apparent Mineralocorticoid
Excess

Arginase Deficiency

Argininosuccinate Lyase
Deficiency

Argininosuccinate Synthetase
Deficiency

Autoimmune Neutropenia

Bile Acid Synthesis Disorders

Carbamyl Phosphate Synthetase
Deficiency

Catastrophic Antiphospholipid Ab
Syndrome

Churg-Strauss Syndrome

Citrin Deficiency

Congenital Adrenal Hyperplasia

Cystic Fibrosis

Episodic Ataxias

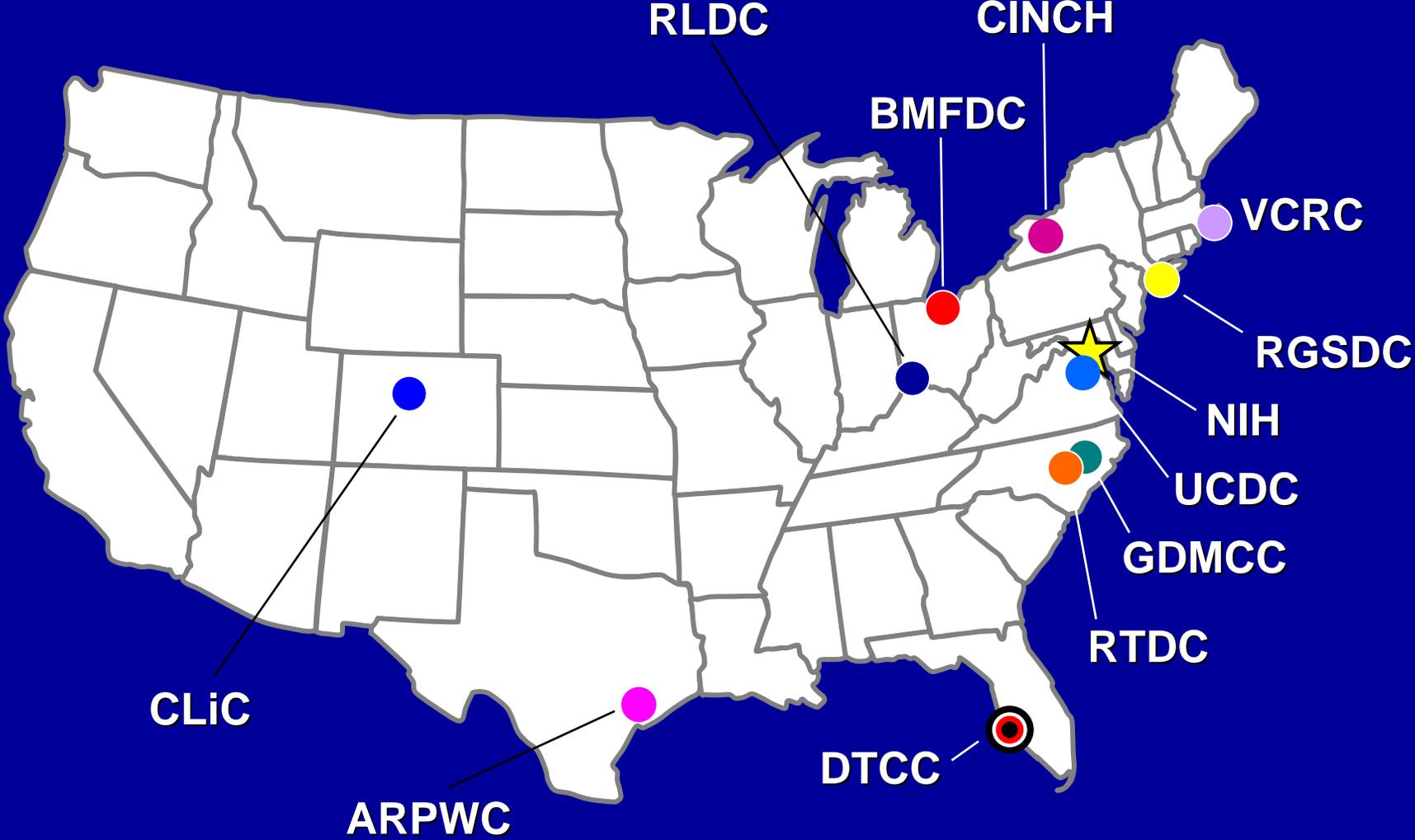
Giant Cell Arteritis

Heparin-induced
Thrombocytopenia

34 Patient Advocacy Groups

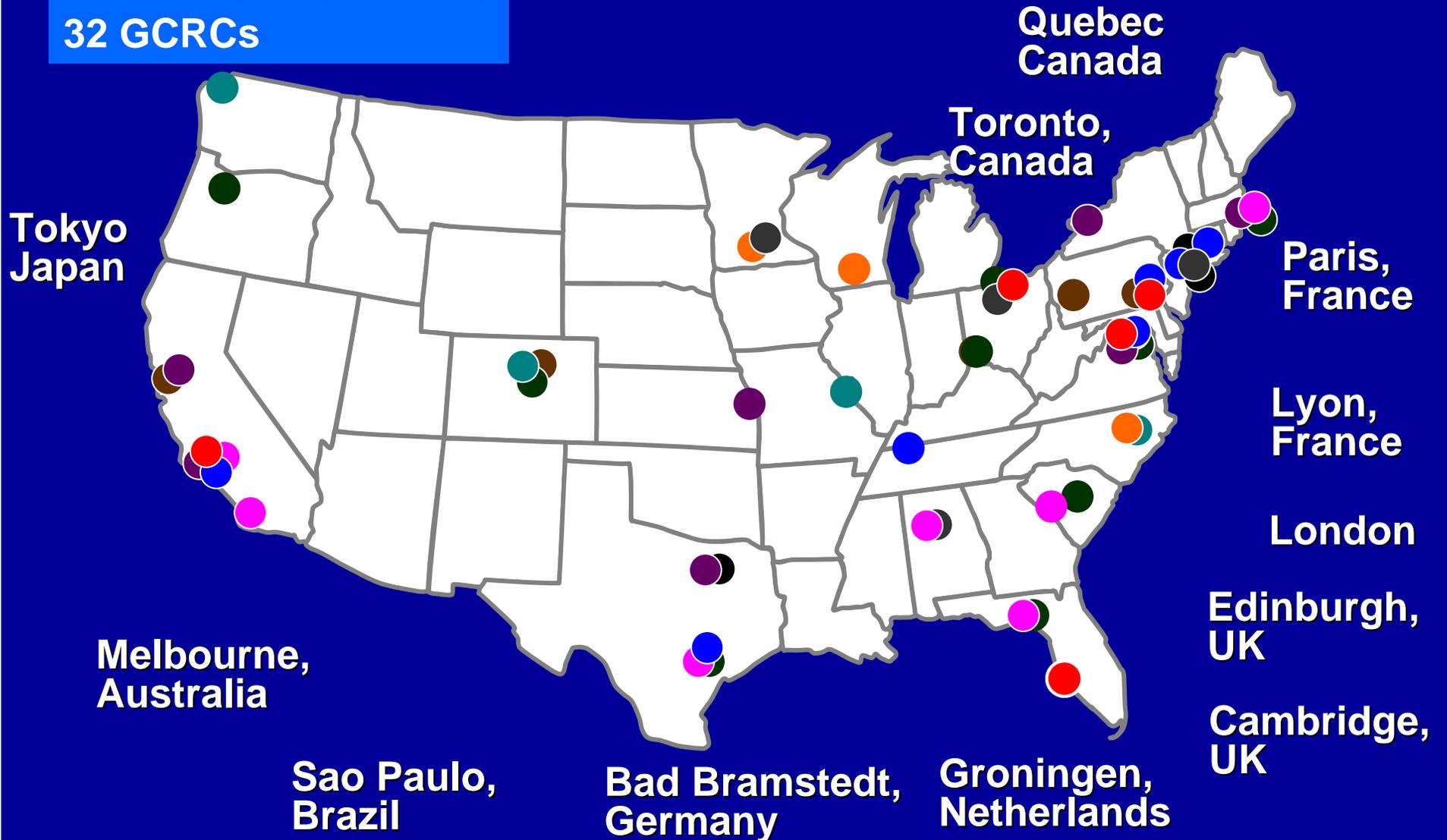
- Alpha-1 Fdn
- Alagille Syndrome Alliance
- American Liver Fdn
- Androgen Insensitivity Support Group
- Angelman Syndrome Fdn
- Aplastic Anemia and MDS International Fdn
- CARES Fdn
- Churg-Strauss Syndrome Assn
- Children's Liver Assn for Support Services
- Children's Liver Disease Fdn
- CSS Patient Group
- Cystic Fibrosis Fdn
- Genetic Alliance
- International Rett Syndrome Assn
- LAM Fdn
- Magic Foundation
- Muscular Dystrophy Assn
- National Adrenal Diseases Fdn
- National Ataxia Fdn
- National Organization for Rare Diseases
- National Urea Cycle Disorders Fdn
- Pediatric Interstitial Lung Disease Family Network Fdn
- Periodic Paralysis Assn
- Platelet Disorder Support Assn
- PNH Support Group
- Polyarteritis Nodosa Support Group
- Prader-Willi Syndrome Assn (USA)
- Primary Ciliary Dyskinesia Fdn
- Pulmonary Alveolar Proteinosis Fdn
- Pulmonary Fibrosis Fdn
- Takayasu's Arteritis Research Assn
- The Angelman Syndrome Fdn
- United Mitochondrial Disease Fdn
- Wegener's Granulomatosis Assn

RDCRN Geographic Distribution - Centers



RDCRN Geographic Distribution - Clinical Sites

55 Medical institutions
32 GCRCs



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
(ORD, NCRR, NIAMS, NICHD, NHLBI, NIDDK, NINDS)

**Coalition of Patient
Advocacy Groups
(CPAG)**

**The Data Technology
Coordinating Center**

**Cholestatic Liver
Disease Consortium**
CLiC



**Rare Lung
Disease Consortium**



- RARE DISEASES
CLINICAL RESEARCH
NETWORK**
- Collaborative Clinical Research
 - Centralized Data Coordination and Technology Development
 - Public Resources and Education
 - Training



**Rare Thrombotic
Diseases
Consortium**

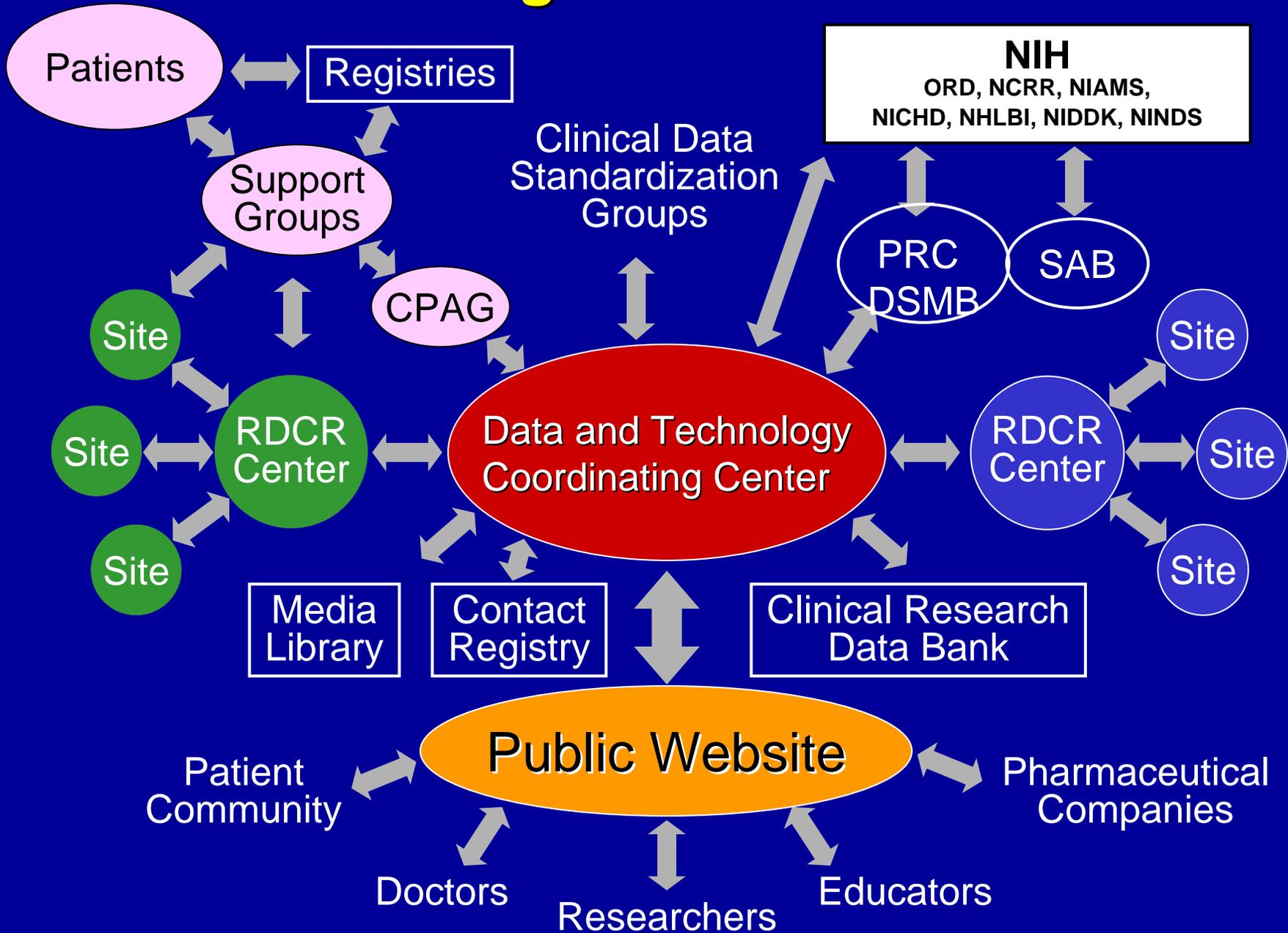
**Rare Genetic Steroid
Disorders Consortium**

**Angelman, Rett and
Prader-Willi Syndromes Consortium**

**Genetic Diseases of
Mucociliary Clearance Consortium**



Integrated Network



Team Work!

- **Clinical Sites**
- **Principal and co-investigators**
- **The DTCC**
- **Trainees**
- **Study Coordinators**
- **Patient Advocacy Groups (PAGs)**
- **NIH staff**
- **Patients**

RDCRN consists of more than 70 sites, more than 30 PAGs and conducts research on ~50 rare diseases!

Progress and Accomplishments



National Standards

- **Use of standardized terminology/ vocabulary (e.g., SNOMED)**
- **Incorporated into protocols, data collection forms and CRFs, database, adverse event reporting, etc.**
- **Innovative data collection techniques**
 - **cell phone call-in and reports by participants that populate database for CINCH**

1. Standardization of Protocol Development and Implementation

- **Standardized Protocol and Consent Formats**
- **Standardized Checklist for submission for approval from DTCC, PRC and DSMB**
- **Manual of Operations template**
- **Protocol Monitoring Plan**
- **Electronic AE and SAE reporting and review**

2. Studies Open and Enrolling

- **Enrolling since Jan., 2006**
- **25 approved protocols**
24 enrolling patients – assistance of PAGs
- **Several studies under development or current review by the PRCs or DSMBs, including:**
 - **Novel therapeutic trials**
 - **Longitudinal studies**
 - **Diagnostic studies**
 - **Demonstration Projects**

Current Participant Accruals

Current Accruals		
Consortium	Total Participants Registered (as of 20/Sep/2006 10:28 PM)	
	Cumulative	Current Year*
Angelman, Rett, & Prader-Willi Syndromes Consortium	44	3
Bone Marrow Failure Disease Consortium	37	2
Consortium for Clinical Investigation of Neurologic Channelopathies	35	0
Genetic Diseases of Mucociliary Clearance Consortium	14	4
Rare Lung Disease Consortium	52	16
Rare Thrombotic Disease Clinical Research Consortium	9	1
Urea Cycle Disorders Consortium	29	0
Vasculitis Clinical Research Consortium	61	9
	281	35

* Current year begins August 1st and ends July 31st

Tracking of Protocol Enrollment

Consortium Members

Email Members

Affiliate Sites



Current Accruals - Participants Registered (as of 20/Sep/2006 10:35 PM)

	Baylor College of Medicine (UCDC)		Children's Hospital of Philadelphia		Children's National Medical Center		Mt Sinai Hospital (UCDC)		University of California at Los Angeles (UCDC)		Vanderbilt University Medical Center		Yale University School of Medicine		Total	
	Cumulative	Current Year*	Cumulative	Current Year*	Cumulative	Current Year*	Cumulative	Current Year*	Cumulative	Current Year*	Cumulative	Current Year*	Cumulative	Current Year*	Cumulative	Current Year*
5101	9	0	1	0	4	0	4	0	3	0	2	0	1	0	24	0
5102	4	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0
5104	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0

* Current year begins August 1st and ends July 31st

Protocol Management Tools

- [5101](#) Longitudinal Study of Urea Cycle Disorders
- [5102](#) The effect of sodium phenylbutyrate (Buphenyl) treatment on the f...
- [5103](#) Carbon-13 Acetate Procedure To Study Ureagenesis
- [5104](#) Assessing Neural Mechanisms of Injury in Inborn Errors of Urea Me...
- [5105](#) N-carbamylglutamate (NCLG) Effect on ureagenesis in N-acetylglut...

3. Interactive Website

- Developed by DTCC
- Accessible and easily navigated
- Provides information about each consortium and each disease
 - for public
 - for caregivers and scientists
- Media Digital Libraries (e.g., lectures, histology)
- Links to useful websites and PAG organizations
- **Contact Registry**

4. Fellows Training

- **35 current or former trainees**
- **Network activities**
 - **Day-long, academic skills workshop for research in rare diseases – Sept., 2007**
 - **Evening poster session and keynote speaker for trainees –Fall, 2007**
 - **Invite Trainees to SC meeting next day – scientific presentations by Consortia**

5. Network Pilot Awards

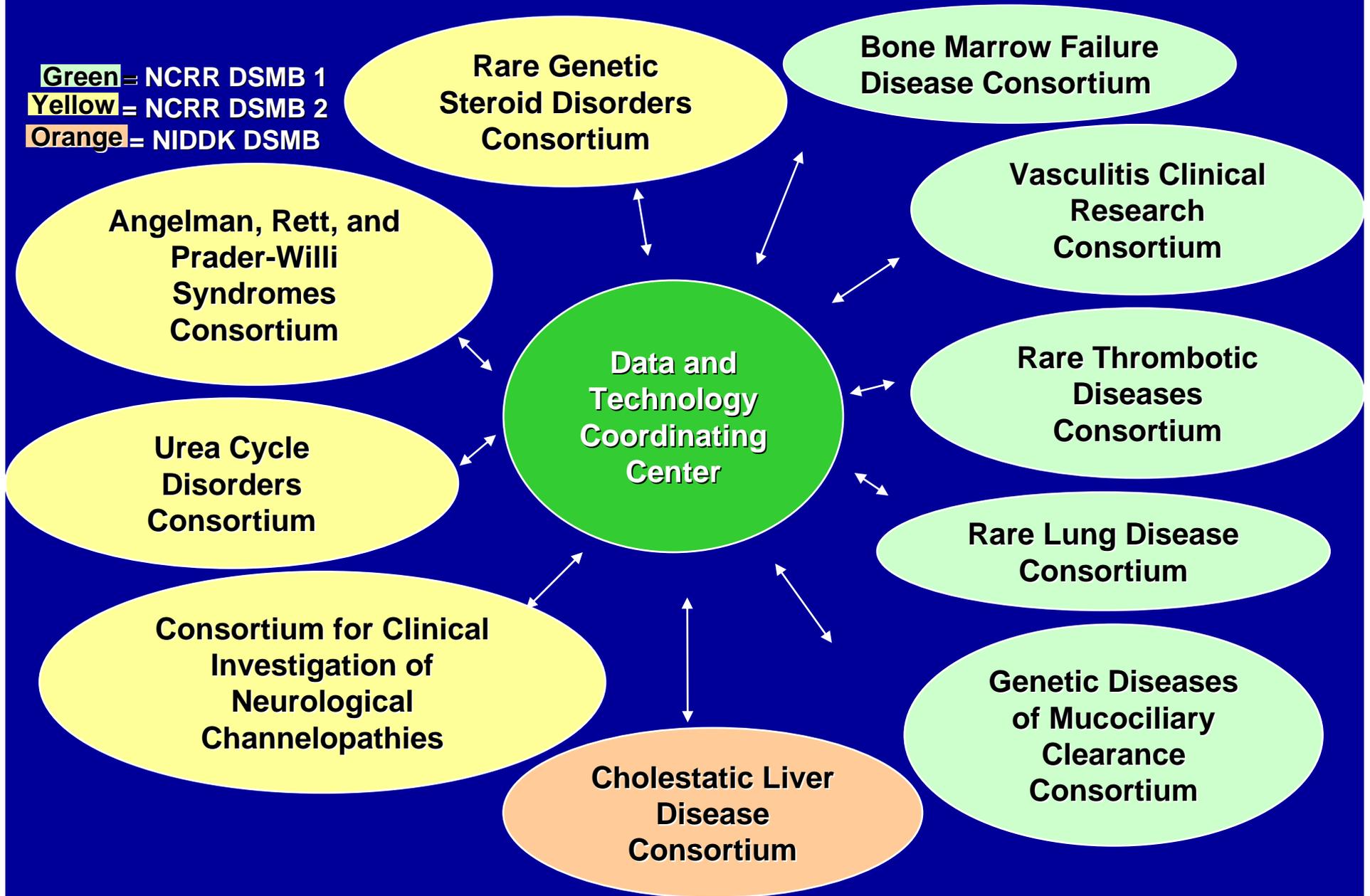
- **New program – 2006-2007**
- **ORD - \$600,000 funds for six pilots – diagnostics or treatment**
- **Each Consortium could submit one application**
- **Steering Committee review – awarding decision**
- **Six awarded**
 - e.g., Biomarker study in Urea Cycle Consortium, New molecular techniques for genetic evaluation in ciliary disorders of lung**

Review Process for Protocols

- **Protocol Review Committees (PRCs) and Data Safety Monitoring Boards (DSMBs)**
- **Consortium and disease-specific expertise**
- **Six PRCs**
- **Three DSMBs**

RARE DISEASES CLINICAL RESEARCH NETWORK DSMBs

Green = NCRR DSMB 1
Yellow = NCRR DSMB 2
Orange = NIDDK DSMB



ORD collaborates with....

- *Existing partners at NIH.....*

NCRR,

NHLBI,

NIAMS,

NICHD,

NIDDK,

NINDS

- *Reissuance of RDCRN RFA*

Intent to Publish a Request for Applications (RFA) for the Rare Diseases Clinical Research Consortia

- Notice published in the NIH GUIDE <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-062.html>
- Details will be published in the RFA.
- 2003 RFA <http://grants.nih.gov/grants/guide/rfa-files/RFA-RR-03-008.html>
- <http://rarediseases.info.nih.gov/> For more information on existing RDCRN check the links under “Research and Clinical Trials”.
- Looking for NIH IC partners!

Office of Rare Diseases National Institutes of Health

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Room 3B-01, MSC - 7518

Bethesda, MD 20892-7518

Voice: 301-402-4336

Fax: 301-480-9655

E-mail: ORD@nih.gov

Website: <http://rarediseases.info.nih.gov/>



Thank you!



Data Technology Coordinating Center (DTCC)

PI: Jeffrey Krischer, Ph.D.

Audrey C. Shor, Ph.D., M.P.H.

**Pediatrics Epidemiology Center
University of South Florida
Tampa, Florida**



What is the DTCC?

- **A coordinated clinical data management system for the collection, storage and analysis of data from multiple diseases and multiple clinical sites**
- **Provides a network website that serves as the framework for public access to the network and secure access for a coordinated clinical data management system for the RDCRCs**



Programmatic Goal

The intention of the NIH is that the data collected within this network become a resource for the Rare Disease Community and be made available to the scientific community.



DTCC Objectives

- **Scalable, coordinated, clinical data management system for collection, storage, and analysis of data of RDCRCs**
- **Portal and tools for integration of developed and publicly available datasets for data mining at RDCRCs**
- **Web based recruitment and referral tools**
- **User friendly resource site for the public, research scientists and clinicians**



Interactive Website

- <http://rarediseasesnetwork.epi.usf.edu/>
- <http://usfpeds.hsc.usf.edu/divisions/biopec/index.htm>





Where do I need to go

Welcome! You have reached the home page for the Rare Diseases Clinical Research Network (RDCRN). Each Consortium within the network provides detailed information on several rare diseases.

What if I am unsure of which consortium to visit?

Scan the list to the right for a disease name. Once you have located it, click on the link for a brief description which will lead you to the correct consortium.

How will this consortium be useful to me?

You can take action! Once you have reached the correct consortium, you will be able to **join the contact registry** for clinical research trials. You will also find several helpful resources that include participating clinical center information, support and advocacy group information and other useful links.



Get information on current open studies and updates on future studies

RDCRN Consortium Studies are opening! [Learn More >>](#) Last Updated: 30 March

■ Clinical Research Consortia :

[Urea Cycle Disorders Consortium \[Study Information\]](#)

N-Acetylglutamate Synthase (NAGS) Deficiency
 Carbamyl Phosphate Synthetase (CPS) Deficiency
 Ornithine Transcarbamylase (OTC) Deficiency
 Argininosuccinate Synthetase Deficiency (Citrullinemia I)
 Citrin Deficiency (Citrullinemia II)
 Argininosuccinate Lyase Deficiency (Argininosuccinic Aciduria)
 Arginase Deficiency (Hyperargininemia)
[Ornithine Translocase Deficiency \(HHH\) Syndrome](#)

[Angelman, Rett, and Prader-Willi Syndromes Consortium \[Study Information\]](#)

Angelman Syndrome
 Rett Syndrome
 Prader-Willi Syndrome

[CINCH - Consortium for Clinical Investigation of Neurological Channelopathies \[Study Information\]](#)

Andersen-Tawil Syndrome (a form of Periodic paralysis)
 Episodic Ataxias
 Non-dystrophic Myotonic Disorders

[Bone Marrow Failure Disease Consortium \[Study Information\]](#)

Aplastic Anemia
 Myelodysplastic Syndromes
 Paroxysmal Nocturnal Hemoglobinuria (PNH)

[Vasculitis Clinical Research Consortium \[Study Information\]](#)

Wegener's Granulomatosis (WG)
 Microscopic Polyangiitis (MPA)
 Churg-Strauss Syndrome (CSS)
 Polyarteritis Nodosa (PAN)
 Takayasu's Arteritis (TAK)
 Giant Cell (Temporal) Arteritis (GCA)

[Rare Genetic Steroid Disorders Consortium \[Study Information\]](#)

Congenital Adrenal Hyperplasia
 Androgen Receptor Defects
 Apparent Mineralocorticoid Excess (Low Renin Hypertension)

[Rare Thrombotic Diseases Consortium \[Study Information\]](#)

Antiphospholipid Antibody Syndromes (APS)
 Heparin-induced Thrombocytopenia (HIT)
 Paroxysmal Nocturnal Hemoglobinuria (PNH)
 Catastrophic Antiphospholipid Antibody Syndrome (Thrombotic Storm)
 Thrombotic Thrombocytopenic Purpura (TTP)

[Rare Lung Diseases Consortium \[Study Information\]](#)

Hereditary Interstitial Lung Disease (hILD)
 Lymphangioleiomyomatosis (LAM)
 Pulmonary Alveolar Proteinosis (PAP)
 Alpha-1 Antitrypsin Deficiency (Alpha-1)

[Genetic Diseases of Mucociliary Clearance Consortium \[Study Information\]](#)



Angelman, Rett & Prader-Willi Syndromes Consortium



Welcome! The Angelman, Rett, and Prader-Willi Syndrome Consortium (ARPWSC) is an integrated group of academic medical centers, patient support organizations, and clinical research resources dedicated to conducting clinical research in genetic and neurodevelopmental disorders. It is our goal to improve the care of patients with Angelman Syndrome, Prader-Willi Syndrome, and Rett Syndrome.

What can I do?

Take Action. Learn more about joining our registry. Research offers no guarantees, but one thing is for certain, research cannot move forward without your help. Every active role a patient takes may possibly part in discovering new groundbreaking research and finding new treatments. [Learn More>>>](#)

What is the Angelman, Rett and Prader-Willi Syndromes Consortium?

[Learn More](#)

[Take Action](#)

[Information for Physicians](#)

[News & Events](#)

[Participating Clinical Centers](#)

[Contact Information](#)



Family & Friends
[::LearnMore](#)



The Disorders We Study:

- Angelman Syndrome
- Rett Syndrome
- Prader-Willi Syndrome

[Term Glossary](#)

[Frequently Asked Questions](#)

Get Involved
[::TakeAction!](#)



Join
the contact registry

[Why Your Participation Matters](#)

[Learn About Current Research Studies](#)

[Find Support or Advocacy Groups in Your Area](#)

Physicians
[::LearnMore](#)



[Syndrome Definitions](#)

[Other Helpful Resources](#)

Research: [Participating Clinical Sites](#)

Download: [Contact Registry Paper Form](#)

In the News:

May 5, 2006 Press Release: [NIH Launches Clinical Studies Nationwide to Investigate Rare Diseases](#)

[RDCRN Makes Contact Registry Available for Download to Facilitate Those Without Internet Access!](#)

ABC News: [Rare Disorder Causes Endless Hunger: Prader-Willi Sufferers Struggle With Uncontrollable Appetite](#)

Network Open Studies

24 open studies:

Cumulative Registrations

4-18-06 9-4-06 4-16-07

Angelman, Rett, & Prader-Willi
Syndromes Consortium (4)

104 334 650

Bone Marrow Failure Disease
Consortium (5)

5 92 183

Consortium for Clinical Investigation
of Neurologic Channelopathies (2)

4 27 83

Urea Cycle Disorders Consortium (3)

12 45 123

Vasculitis Clinical Research
Consortium (5)

1 24 139

Genetic Diseases of Mucociliary
Clearance Consortium (2)

39 137

Rare Lung Disease Consortium (1)

6

Cholestatic Liver Consortium (0)

Rare Thrombotic Disorders Consortium (1)

212

Genetic Steroid Disorders Consortium (1)

Total: 126 561 1533

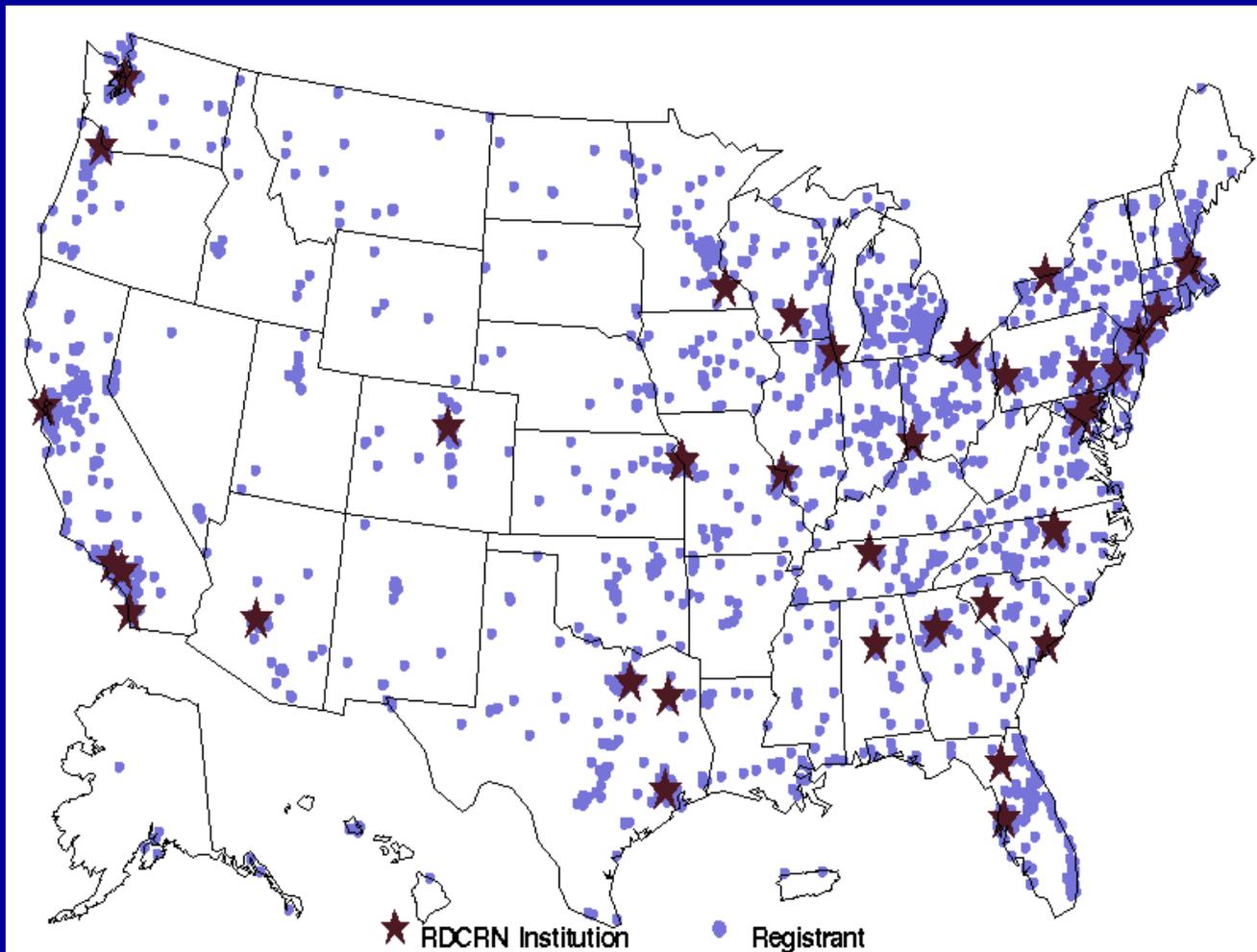
Contact Registry Enrollment

Consortium

	Registrations	
	4-19-06	4-16-07
Angelman, Rett, & Prader-Willi Syndromes Consortium	298	508
Bone Marrow Failure Disease Consortium	57	207
Consortium for Clinical Investigation of Neurologic Channelopathies	22	77
Urea Cycle Disorders Consortium	159	219
Vasculitis Clinical Research Consortium	926	1374
Genetic Diseases of Mucociliary Clearance Consortium	61	201
Rare Lung Disease Consortium	20	210
Cholestatic Liver Consortium	97	178
Rare Thrombotic Disorders Consortium	86	223
Genetic Steroid Disorders Consortium	4	34

Total : 1730 3231

Contact Registry and RDCRN



DTCC Features

- **Multi-center, multi-national, multi-disciplinary studies**
- **Web-based data collection**
- **Management of large, diverse data bases**
- **Clinical trials**
- **Epidemiology studies**



DTCC Features

- **Live webcasts**
- **Internet-based videoconferencing**
- **Video libraries**
- **Electronic data exchange with labs and remote sites**
- **Interactive voice response systems for registration/randomization**



DTCC Features

- **Organize and schedule steering committee meetings**
- **Clearinghouse for network materials and protocols**
- **Development of public websites and interface with outside groups**
- **Organize/distribute materials for DSMB**



Collaboration: Clinical Research

- Longitudinal studies of individuals with rare diseases
- Clinical studies
- Phase one and two trials
- Pilot and demonstration projects

Design, implementation, data collection, analysis and publication of studies



Collaboration: Training

- Training of clinical investigators in rare diseases research.

Application of web-based video streaming to include video libraries, and “ask the professor” conferences; links to other resources



Collaboration: Distributed Data Management

- **Develop a test bed for distributed clinical data management that incorporates novel approaches and technologies for**
 - data management,
 - data mining,
 - data sharing across rare diseases, data types, and platforms;
- **Provide access to information related to rare diseases for basic and clinical researchers, academic and practicing physicians, patients, and the lay public.**

Web-based data mining tools



Collaboration: Web-Based Resources

- A portal and tools for integration of developed and publicly available datasets for data mining at RDCRCs,
 - Web based recruitment and referral
 - User friendly resource site for the public, research scientists, and clinicians.

Interactive systems



In Summary...

The DTCC strives to provide services and technology to enable clinical studies to recruit, gather and analyze data, and facilitate collaboration between investigators throughout the US and international communities.





<http://rarediseasesnetwork.epi.usf.edu/>

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Genetic and Rare Diseases Information Center

- **The Genetic and Rare Diseases Information Center (GARD) information specialists provide individually tailored information to patients and their families, health professionals, researchers, and to the public.**
- **Since 2002, GARD has responded to more than 16,000 inquiries for more than 4,732 rare and/or genetic diseases**

The Genetic and Rare Diseases Information Center

- ❑ 6,740 Related Terms
- ❑ Next Step – National Library of Medicine Collaboration
- ❑ Toll-free 1-888-205-3223 (USA)
- ❑ International Access Number: 301-519-3194
- ❑ Fax: 240-632-9164
- ❑ E-mail: GARDinfo@nih.gov

NIH ANNOUNCES LICENSING OPPORTUNITIES FOR RARE DISEASE TECHNOLOGIES

(Dec. 2006)

- **This new resource was developed by the Office of Rare Diseases and the Office of Technology Transfer (OTT) at the NIH.**
- **<http://www.ott.nih.gov/rarediseases>**
a new website offering technologies available for commercial licensing that are related to rare diseases or conditions.
- **this new site will help facilitate the transfer of research advances from bench to bedside where the interventions can ultimately benefit patients**

- **consists of more than 500 such technologies, including drugs, biologics, and devices, available to be transferred from the NIH and the U.S. Food and Drug Administration (FDA) to the private sector for further research and development and potential commercialization.**
- **we encourage not-for profit organizations, academic research centers and foundations in the U.S. and abroad to submit technologies available for licensing from their institutions**
- **Parties interested in licensing will be directed to the institution owning the technology. More information about submitting additional technologies can be found at <<http://www.ott.nih.gov/rarediseases/submit>>.**

Database of Biospecimen Repository

- **The goal is to facilitate research leading to treatments and cures for rare diseases by improving researchers' access to needed human biological materials (HBM) via an interactive, comprehensive database that is**
 - **accessible via a Web browser,**
 - **is searchable online, and**
 - **contains detailed information about repositories that collect, store, and distribute HBM for research use in the United States.**

Objectives

- **Facilitate researchers' access to HBM for use in research by providing a system that enables them to access information about repositories and their collections.**
- **Create a publicly accessible, searchable, Web-based database of repositories that collect, store, and distribute human biological materials for research use.**
- **Identify unmet needs of researchers in obtaining HBM for research on rare diseases.**
- **Provide information to researchers and the wider research community and other interested parties about the types and locations of human tissue repositories and the HBM available for research purposes.**

ORD: Scientific Conferences Program

- Identify Research Opportunities
- ❑ Establish Research Priorities
- ❑ Develop Program Announcements and Solicit R01 Applications
- ❑ Establish Diagnostic and Monitoring Criteria
- ❑ Develop Animal Models
- ❑ Support Registries - Patient and Tissue
- ❑ Develop Research Protocols, Collaborative Research Arrangements, and Plan Clinical Trials
- ❑ Disseminate Results to Targeted Professional and Voluntary Health Organizations
- ❑ Co-Sponsor with Patient Advocacy Groups, Academic Investigators, Industry, Foundations, Intramural and Extramural Research Programs

ORD “CETT” Program

- Collaboration*
- Education*
- Test (Genetic)*
- Translation*
- Program for Rare Genetic Diseases
- Dr. Roberta Pagon, Andrew Faucett, Dr. Giovanna Spinella, and Dr. Suzanne Hart

Key Features of CETT

- ❑ Model of Cooperation between researcher, diagnostic laboratory and patient advocate group to translate diagnostic tests from research to a clinical laboratory
- ❑ Flexibility of process to allow for development of different types of genetic tests, collaborations and sources of test development
- ❑ Development of clinical materials and data collection to improve understanding of the genetic test and understanding of the rare disease.

Process

- Application must be submitted by team
 - Patient advocate group
 - Clinical (CLIA-certified) laboratory
 - Researcher (laboratory and/or clinician)
- Preliminary review by Program Coordinator & Program Scientific Advisor

Process

- Application forwarded to Review Board Coordinator
- Reviewed by 4 members of Review Board (clinician, molecular/biochemical geneticist, patient advocate, clinical geneticist)
- Accepted for translation or
- Returned to submission team with questions and suggestions – “facilitated process”

Requirements

- Information about the correlation between the disease and the test
- Information about the potential impact of the test on healthcare management
- Evidence that the clinical lab is experienced in diagnostic testing (e.g., number of tests, experience of staff, genetic counselors, CLIA certification)
- Proposed method(s) of testing is the most appropriate methods for the disorder
- Projections for cost of tests set-up and charge for individual test

Requirements

- ❑ Statement of collaborative commitments between researcher, clinical lab and advocacy group
- ❑ Educational materials in a standardized format for clinical care providers and for patients to address correlation between the disease and the test, potential impact of the test on healthcare management, test ordering, test interpretation, and the benefits and risks of testing

Requirements

- ❑ Phenotype / genotype data collection plan to improve understanding of the disease and test interpretation including the method of storage for the phenotype and genotype data
- ❑ Annual report form on volume of testing, detection rate, mutations found to be used to update “Gene Reviews”

Goals of Global Approach to Rare Diseases and Orphan Products

- ❑ Mobilize Health Professionals and Society to Take Action**
- ❑ Obtain Cooperative and Collaborative Support From All Nations and Partners in Health Research and Product Development**
- ❑ Improve Health Literacy of Populations to Enable Information-Based Decision Making**
- ❑ Reduce Disparities in Global Health with Ready Access to Information and Interventions for Diagnosis, Prevention, and Treatment of Rare Diseases**

Benefits of Rare Diseases Research and Orphan Products Development

- ❑ More Rapid Access to Investigational and Approved Orphan Products to Meet Patient and Family Needs**
- ❑ Improved Information Development and Dissemination Activities**
- ❑ Establish Collaborative and Cooperative Research Partnerships (Multiple Principal Investigators on Grants)**
- ❑ Reduce Time to Diagnosis and Improve Genetic Testing Procedures**
- ❑ Quicker and Less Expensive Development of Orphan Products**

Coordinated Efforts for Successful Orphan Products Development/Rare Diseases Research

- Pharmaceutical, Biotechnology, and Medical Devices Industries
- Academic and Private Foundation Research Communities-
Multidisciplinary Research Efforts
- Medical Specialty Societies and Healthcare Providers
- Patient Advocacy Groups
- Federal Government
 - Regulatory
 - Reimbursement
 - Research
 - Health Care Services
 - Prevention

Quicker and Less Expensive Development of Safe and Effective Orphan Products

- Provide Global Access to Clinical Studies and Clinical Trials of Private and Public Sectors**
- Develop Globalization of Research Efforts and Common Protocols with Multidisciplinary Research Teams**
- Continue Efforts for Harmonization of Research Data for Regulatory Purposes**
- Natural History Studies to Establish Better Definitions of Patient Responders with Development of Appropriate Biomarkers and Surrogate Endpoints for Safety and Efficacy**
- Utilize Screening Processes of Industry and Government Chemical Libraries**

Obtaining the Correct Diagnosis and Improving Dissemination of Information About Rare Diseases and Orphan Products

- ❑ *Expansion of Newborn Screening Programs*
- ❑ Increased Development of Genetic and Diagnostic Tests with Appropriate Patient and Family Counseling
- ❑ Increase Educational Efforts for the Public and Health Care Providers' Communities
 - ❑ Better Diagnostic Criteria for Rare Diseases
 - ❑ Available Treatments for Specific Diseases
 - ❑ Standards of Care for Emergency and Critical Care Treatments
- ❑ Expand Global Linkages and Collaborations of Patient Advocacy Group Networks
- ❑ Develop Inclusive Web-Based Inventory of Global Rare Diseases Research Studies/Intervention Activities and Information Resources
- ❑ NLM- ClinicalTrials.gov

Promoting Quality Genetic Testing

- Gaining Acceptance of Global Testing Services and Certification Standards
- Interpretation of Results with Appropriate Patient Counseling
- Foster Development of Collaboration, Education, and Genetic Test Translation Program - (CETT) Prototype
- Genome-Wide Association Studies - RFI
- <http://grants.nih.gov/grants/gwas/index.htm>
- Establish Partnerships and Networks to Improve Research Translation and Data Sharing
 - Between and among research and clinical laboratories

Meeting Patient and Family Needs

- Identify Economic Impact of Rare Diseases on Families and Individuals
- Expand Training Programs for PAG on Living and Coping with Rare and Genetic Diseases
- Gaining Acceptance for Disabilities and Improving Educational Opportunities for Patients
- Maximize Access to Rehabilitation Therapies – Physical, Hearing, Speech, Vocational, Occupational
- Provide Worldwide Access to Safe and Effective Products for the Prevention, Diagnosis, and Treatment of Rare Diseases
- Provide Ready Access to Information About Rare Diseases

ORD Present and Future Emphasis and Needs

- Genetic Testing – CETT Program
- Inventory of Bio-specimen Collection, Storage, and Distribution Repositories (Biobanks)
- Need for Patient/Research Registry Standards
- Develop Acceptable Method of Determining Prevalence of Rare Diseases
- Bench to Bedside Grant Program – IRP/ERP
 - <http://clinicalcenter.nih.gov/ccc/btb/awards.shtml>
- Office of Technology Transfer (Neglected Diseases, Rare Diseases) Available Technology from Government (>750 technologies) and Academic Laboratories and Clinics (Future)
- Patient Travel – Angel Flight
- Undiagnosed Diseases

Items of Interest from ORD/NIH

- ❑ **Genome-Wide Association Studies - RFI on Genome Wide Association Studies. Submit genetic data (genotype) with Relevant health Information (Phenotypes) to a Central Data Repository**

- <http://grants.nih.gov/grants/qwas/index.htm>

- ❑ **Annual Report on Rare Diseases Research Advances
Office of Rare Diseases, National Institutes of Health**

- http://rarediseases.info.nih.gov/html/reports/fy2005/Annual_Report_FY_05_Final.pdf

- ❑ **Multiple Principal Investigators web site:**

- http://grants.nih.gov/grants/multi_pi/index.htm

ORD Website

<http://rarediseases.info.nih.gov/>

- Rare Diseases Information – Pub Med
- Research and Clinical Trials - CRISP, ClinicalTrials.gov
- Patient Support Groups - DIRLINE > 1200 Patient Advocacy Groups, NORD, Genetic Alliance
- Patient Travel & Lodging
- Genetics Information – Gene Tests, OMIM, NCHPEG
- Research Resources
- Scientific Workshops, Archived Reports

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