Activities of the Office of Rare Diseases Research

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Office of Rare Diseases Research (ORDR)
National Center for Advancing Translational Science (NCATS)
National Institutes of Health (NIH)
Department of Health and Human Services
June 21, 2012
US Research on Rare Diseases
Sixth Willi-Kühne-Lecture:
Center for Rare Diseases Research
Ulm, Germany

Rare Diseases: Window on Nature?

Nature is nowhere accustomed more openly to display her secret mysteries than in cases where she shows traces of her workings apart from the beaten path; nor is there any better way to advance the proper practice of medicine than to give our minds to the discovery of the usual law of nature, by the careful investigation of cases of rarer forms of disease.

~ William Harvey, Letter IX,
to John Vlackveld, *24 Apr 1657*

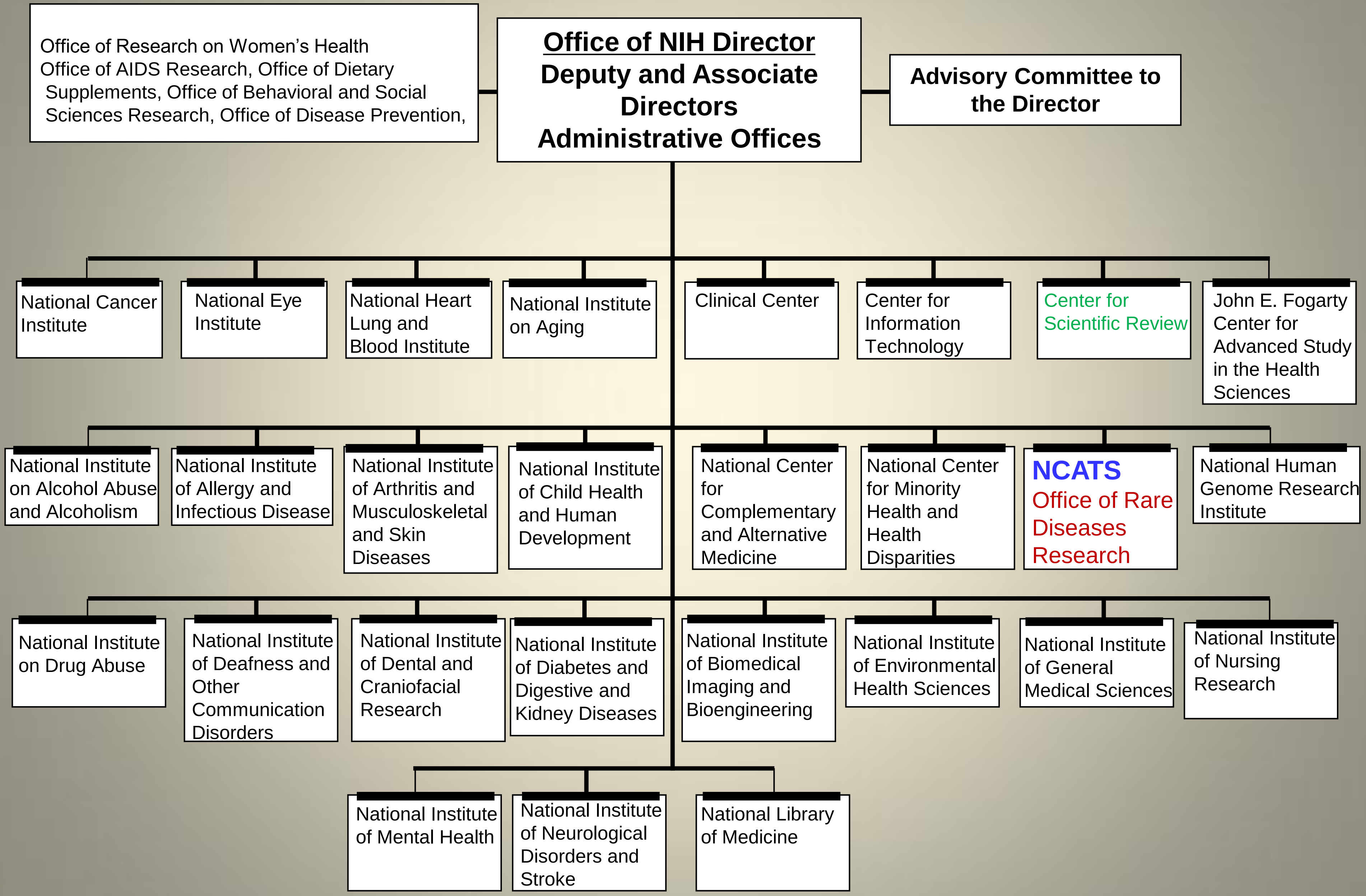
Why The Increased Interest in Rare Diseases and Orphan Products?

- Public Recognition that Rare Diseases Represent a Global Public Health Issue
- Public and Media Interest
- Increased Number of Research Investigators Experienced in Rare Diseases Multi-Center, International Clinical Trials
- Improved Patient Recruitment is Possible
- Expanded Roles of Patient Advocacy Groups
- Public-Private Partnerships Increasing

Why The Increased Interest in Rare Diseases and Orphan Products?

- Increased Industry Interest in Niche Markets
- Opportunities for Repurposing of Approved and Investigational Products
- Better Models Available for Research Design with Small Patient Populations
- Expanding Federal, National, and International Interest and Support
- Development of More Directed Research Agenda Leading to Interventions and Diagnostics
- Increase in Scientific Opportunities

The View of the NIH



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National Institute on Aging

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National Institute on Alcohol Abuse and Alcoholism

National Institute of Allergy and Infectious Disease

National Institute of Arthritis and Musculoskeletal and Skin Diseases

National Institute of Child Health and Human Development

National Center for Complementary and Alternative Medicine

National Center for Minority Health and Health Disparities

NCATS
Office of Rare Diseases Research

National Human Genome Research Institute

National Institute on Drug Abuse

National Institute of Deafness and Other Communication Disorders

National Institute of Dental and Craniofacial Research

National Institute of Diabetes and Digestive and Kidney Diseases

National Institute of Biomedical Imaging and Bioengineering

National Institute of Environmental Health Sciences

National Institute of General Medical Sciences

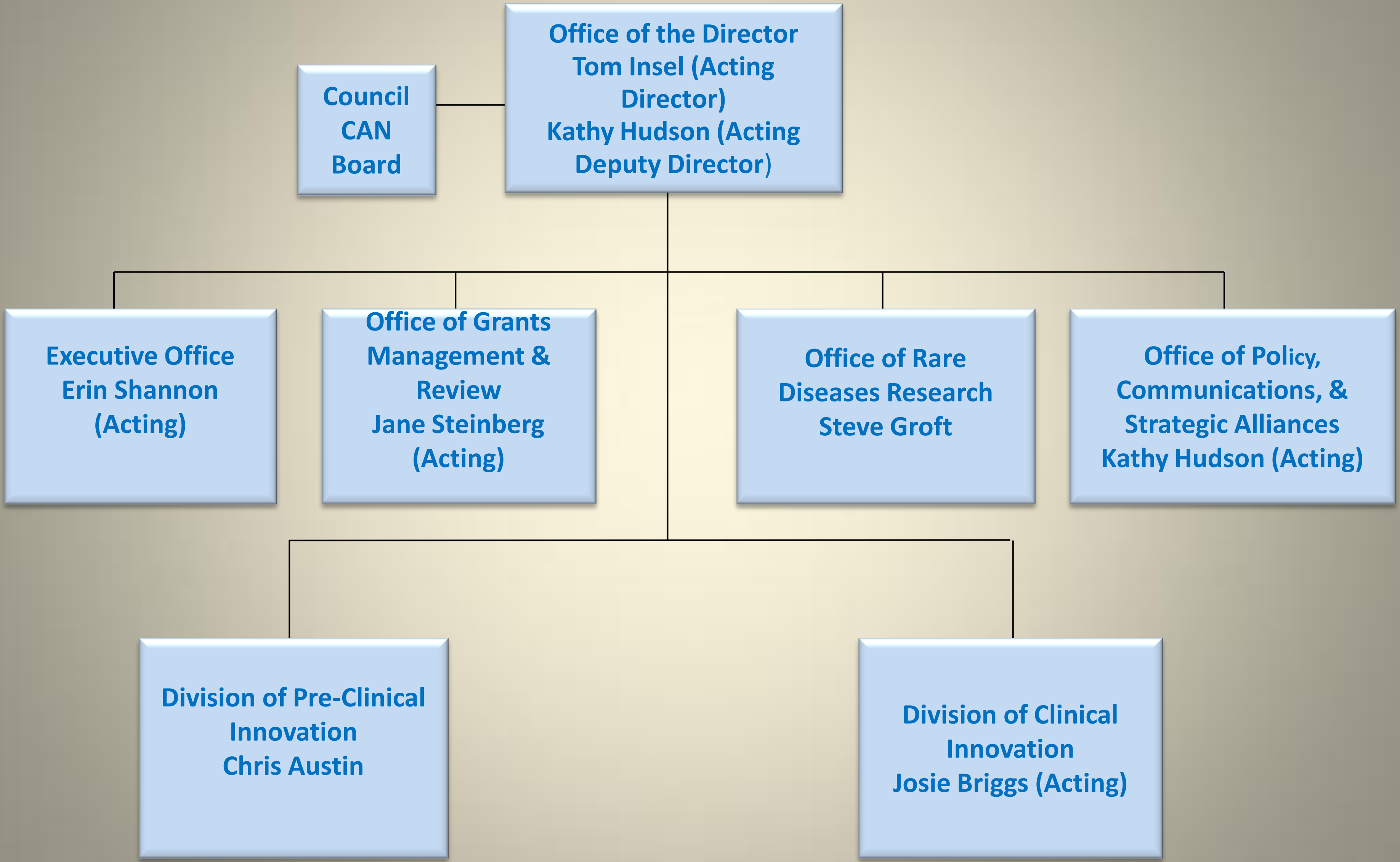
National Institute of Nursing Research

National Institute of Mental Health

National Institute of Neurological Disorders and Stroke

National Library of Medicine

National Center for Advancing Translational Sciences (NCATS)



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Creation of the National Center for Advancing Translational Sciences (NCATS)

To catalyze the development of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions

Selected NIH Translational Research Programs and Resources

- NCATS – Division of Preclinical Innovation
  - Therapeutics for Rare and Neglected Diseases Program
  - Bridging Interventional Development Gaps Programs
  - Chemical Genomics Center
  - Molecular Libraries Program
- NCATS Division of Clinical Innovation
  - Research Match
  - Research Electronic Data Capture (RED Cap)
  - The CTSA Pharmaceutical Assets Portal
- NCI
  - NCI Experimental Therapeutics (NExT) Program
  - Regulatory Assistance Program
  - Investor Forum
- NINDS
  - NeuroNEXT

Selected NIH Translational Research Programs and Resources

- NIAID
  - Division of Microbiology and Infectious Diseases
  - Clinical Research Programs and Networks
  - Clinical Evaluation Resources for Researchers
  - Vaccine Research Center

- NICHD
  - Best Pharmaceuticals for Children Act
  - Newborn Screening Translational Research Network
  - Collaborative Pediatric Critical Care Research Network

- NHLBI
  - Centers for Accelerated Innovation
  - Vascular Interventions/Innovations and Therapeutic Advances
  - Gene Therapy Resources Program
  - Production Assistance for Cellular Therapeutics

- Small Business Grant Awards
  - SBIR - 2.6% of extramural budget and
  - STTR - 0.35% annual set-aside.

NIH Collaborative Efforts

- Integrated Microphysiological Systems for Drug Efficacy, Bioavailability, Toxicology, and Toxicity Testing in Human Health and Disease (Tissue on a Chip)
- http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-11-022.html
- Discovering New Therapeutic Uses for Existing Molecules (Drug Rescue and Repurposing)
  - Match compounds from pharma's "virtual medicine cabinet" with innovative ideas for new indications from NIH extramural scientists
  - 8 companies and ~58 compounds
  - Pfizer, AstraZeneca, Eli Lilly and Company, Abbott, Bristol-Myers Squibb Company, GlaxoSmithKline, Janssen Pharmaceutical Research & Development, L.L.C., and Sanofi
  - **http://www.nih.gov/news/health/jun2012/ncats-12.htm**
  - Memorandum of Understanding – Between NIH and Industry Partners
  - Confidential Disclosure Agreement and Collaborative Research Agreement Templates - Between the Pharmaceutical Company Partner and the Applicant

Office of Rare Diseases Research

- **Web-Based Global Rare Diseases Patient Registry and Data Repository (GRDR)**
  - **http://federalregister.gov/a/2012-03155 Federal Register Request for Information on Feb. 10, 2012**
  - **http://rarediseases.info.nih.gov/files/GRDR_CDEs.pdf**
  - **http://rarediseases.info.nih.gov/PatientRegistry.aspx**
- **Web-Based Searchable Registry of Biospecimen Repositories – In Development**
  - **http://biospecimens.ordr.info.nih.gov/**
- **Research, Condition, Disease Categorization (RCDC) for Rare Diseases and Orphan Drugs FY 2011**
  - **NIH Rare Diseases ~ $ 3.527 Billion (~9400 Research Projects)**
  - **NIH Orphan Drugs ~ $ 749 Million (~1650 Research Projects)**
  - **http://report.nih.gov/rcdc/categories/**
  - **~11.38% of NIH Research Budget**
- **Genetic Testing Registry – Dr. Wendy Rubinstein**
  - **http://www.ncbi.nlm.nih.gov/gtr/**
- Research Match/NCATS - Clinical and Translational Science Awards Program
  - https://www.researchmatch.org/
- Rare Diseases Clinical Research Network Contact Registry

  http://rarediseasesnetwork.epi.usf.edu/registry/index.htm

Office of Rare Diseases Research

- Clinical Center Hospital Bedside to Bench Research Program
  - www. http://clinicalcenter.nih.gov/ccc/btb/index.html
  - http://grants.nih.gov/grants/guide/notice-files/NOT-OD-12-005.html

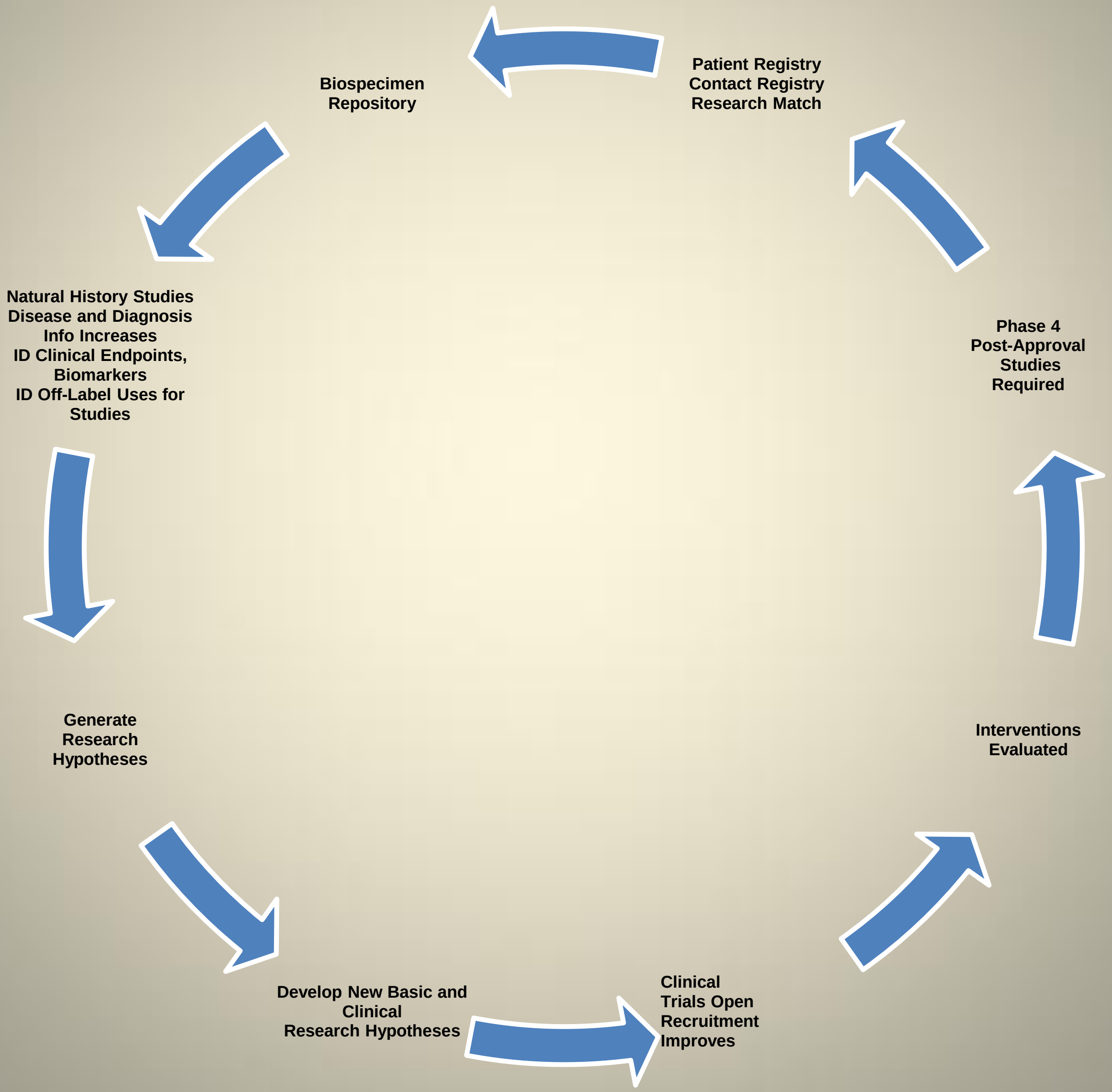
- Scientific Conferences Program – Identify Research Opportunities and Establish Research Agenda (1200 Conferences)
  - http://grants.nih.gov/grants/guide/pa-files/PA-10-071.html

- Middle School Curriculum Module on Rare Diseases and Scientific Inquiry http://science.education.nih.gov/customers.nsf/MSDiseases.htm

- Undiagnosed Diseases Program

- International Classification of Diseases (ICD 11) Orphanet

Developing Pathways to Interventions Through Partnerships



Patient Registry
Contact Registry
Research Match

Biospecimen
Repository

Natural History Studies
Disease and Diagnosis
Info Increases
ID Clinical Endpoints,
Biomarkers
ID Off-Label Uses for
Studies

Generate
Research
Hypotheses

Develop New Basic and
Clinical
Research Hypotheses

Clinical
Trials Open
Recruitment
Improves

Interventions
Evaluated

Phase 4
Post-Approval
Studies
Required

GRDR Project Overview

- 15 GRDR Patient Registries + 19 Existing Registries
- Ability to conduct pan-disease analysis and recruitment
- Share de-identified patient data
- Develop and use rare disease Common Data Elements (CDE)
- Explore integration of EHR into GRDR
- Develop an accessible Web-based registry template
- Establish a public / private partnership model of sustainability
- Evaluate the data mapping, data export/import processes, and data mining capabilities

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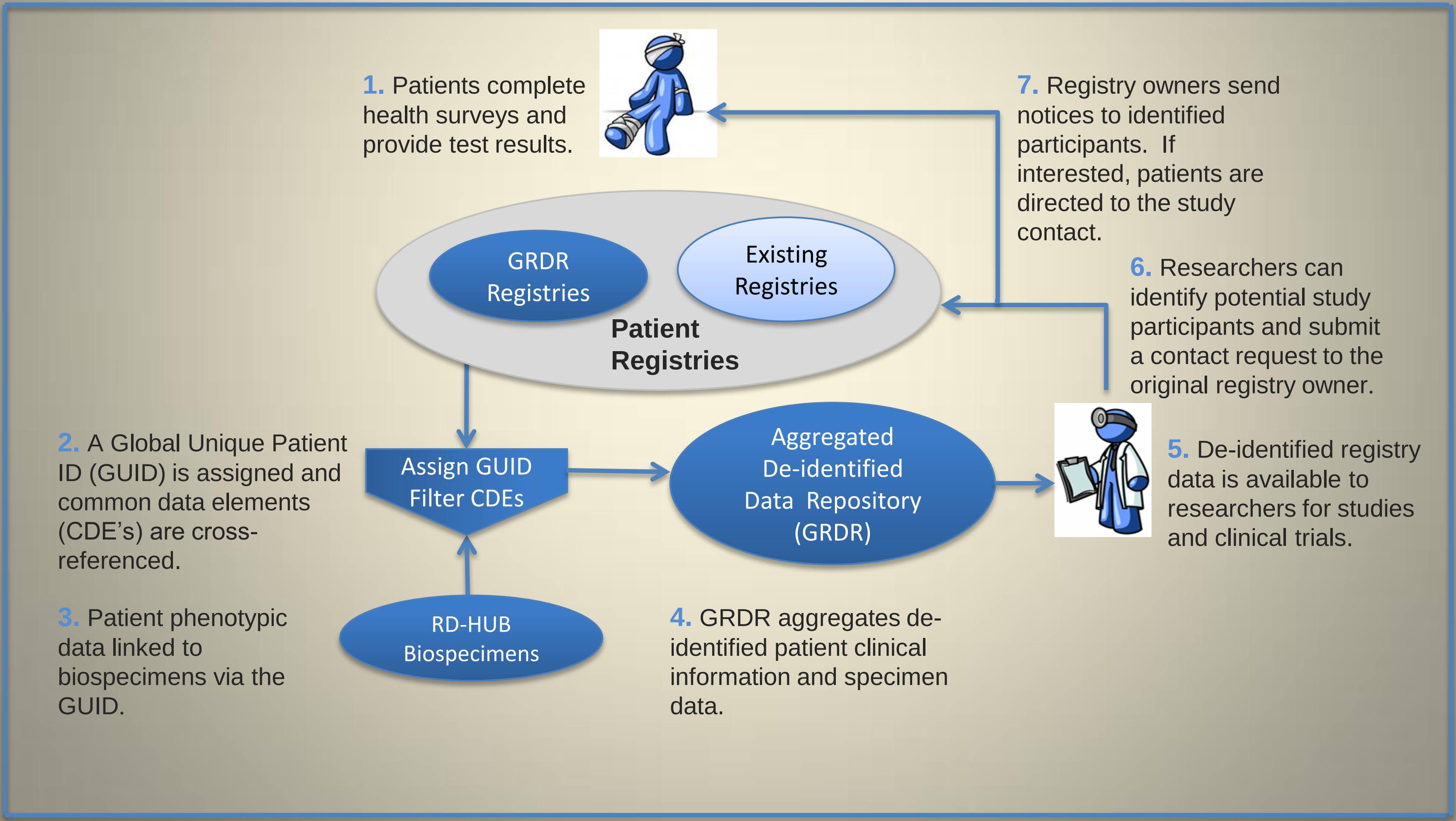
Global Rare Diseases Patient Registry and Data Repository (GRDR)



1. Patients complete health surveys and provide test results.

GRDR Registries

Existing Registries

Patient Registries

2. A Global Unique Patient ID (GUID) is assigned and common data elements (CDE's) are cross-referenced.

Assign GUID
Filter CDEs

3. Patient phenotypic data linked to biospecimens via the GUID.

RD-HUB
Biospecimens

Aggregated
De-identified
Data Repository
(GRDR)

4. GRDR aggregates de-identified patient clinical information and specimen data.

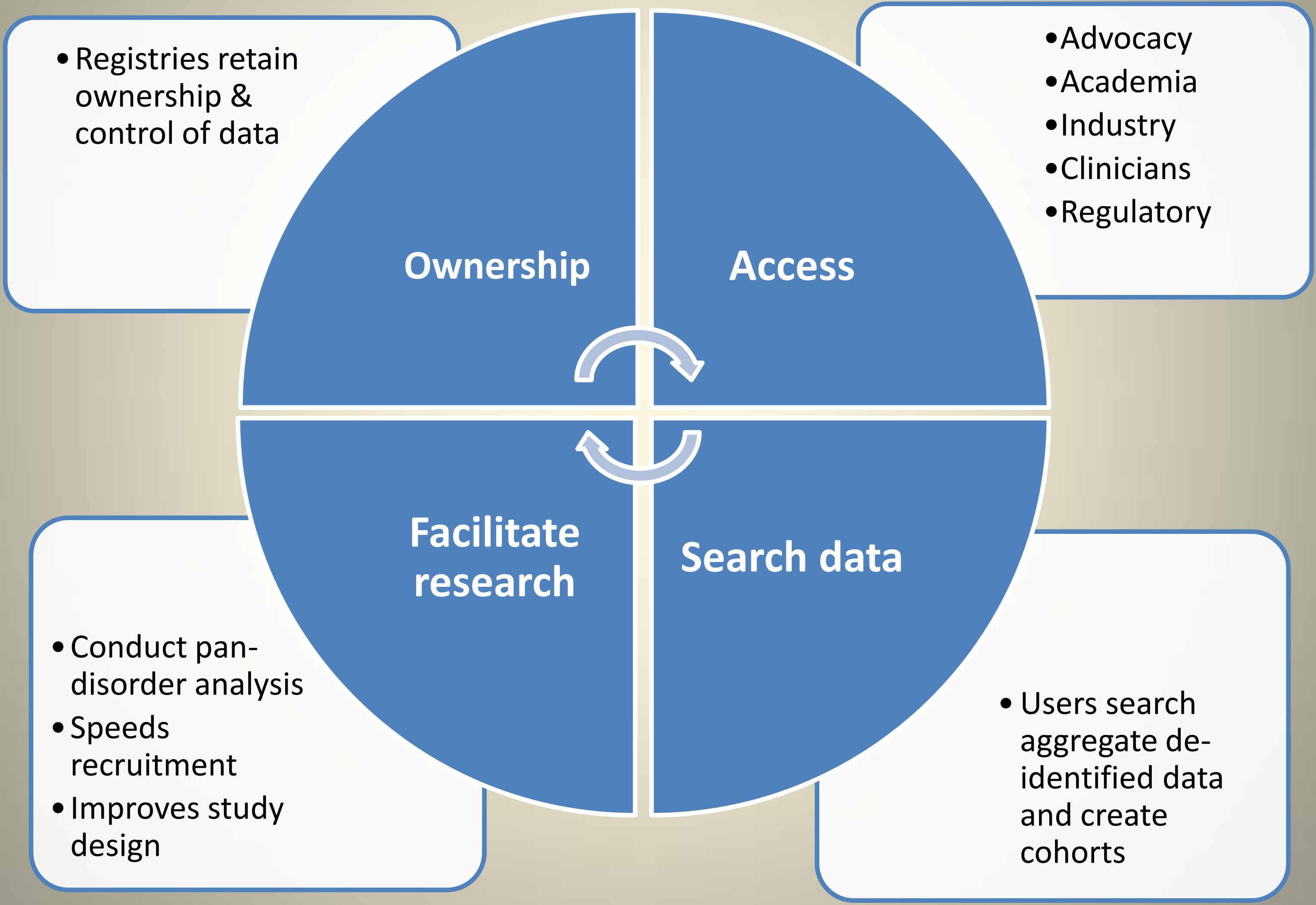
5. De-identified registry data is available to researchers for studies and clinical trials.

6. Researchers can identify potential study participants and submit a contact request to the original registry owner.

7. Registry owners send notices to identified participants. If interested, patients are directed to the study contact.

GRDR Repository:

Participants in the project will retain control and ownership of submitted data, and will contribute to a rare disease resource that promotes community-wide discovery within and across diseases



Ownership

- Registries retain ownership & control of data

Access

- Advocacy
- Academia
- Industry
- Clinicians
- Regulatory

Search data

- Users search aggregate de-identified data and create cohorts

Facilitate research

- Conduct pan-disorder analysis
- Speeds recruitment
- Improves study design

How Can Investigators Participate?

Academia

- Map existing or dormant registry data to CDEs
- Contribute de-identified patient data
- Partner with patient groups to establish registries

Industry Partners

- Join GRDR public-private partnership efforts
- Accelerate adoption by sponsoring registries
- Contribute to self-sustaining business models
- Increase scope and speed of deployment of registries for diseases of interest

Benefits

Stakeholder	Benefits
Patients & Foundations	• Ability to organize patient populations for clinical trials & studies • Patients can learn from others through survey results • Raise visibility to patients and researchers • Complete questionnaires in local language
Pharma / biotech	• Ability to share de-identified pan-disease patient information • Link proprietary information to shared patient record • Ability to share information with patients based on specific profile • Multi-lingual capabilities collect international patient data
Researchers and Academia	• Learn directly from patients and families • Ability to recruit for clinical studies & trials pan-disorder • Gain access to broader pool of clinical candidates • Interactive maps enable clinical trial site planning
Government	• Access to patient reported outcomes • Self-sustaining business model frees funding for other research

Common Data Elements/Questions

- Current contact information
- Socio-demographic information
- Diagnosis
- Family history
- Birth and reproductive history
- Anthropometric information
- Patient-reported outcome
- Medications, devices, and health services
- Clinical research participation and biospecimen donation
- Communication preferences
- Organ systems and disease specific DEs in development
- Contact Yaffa.Rubinstein@nih.gov

Office of Rare Diseases Research

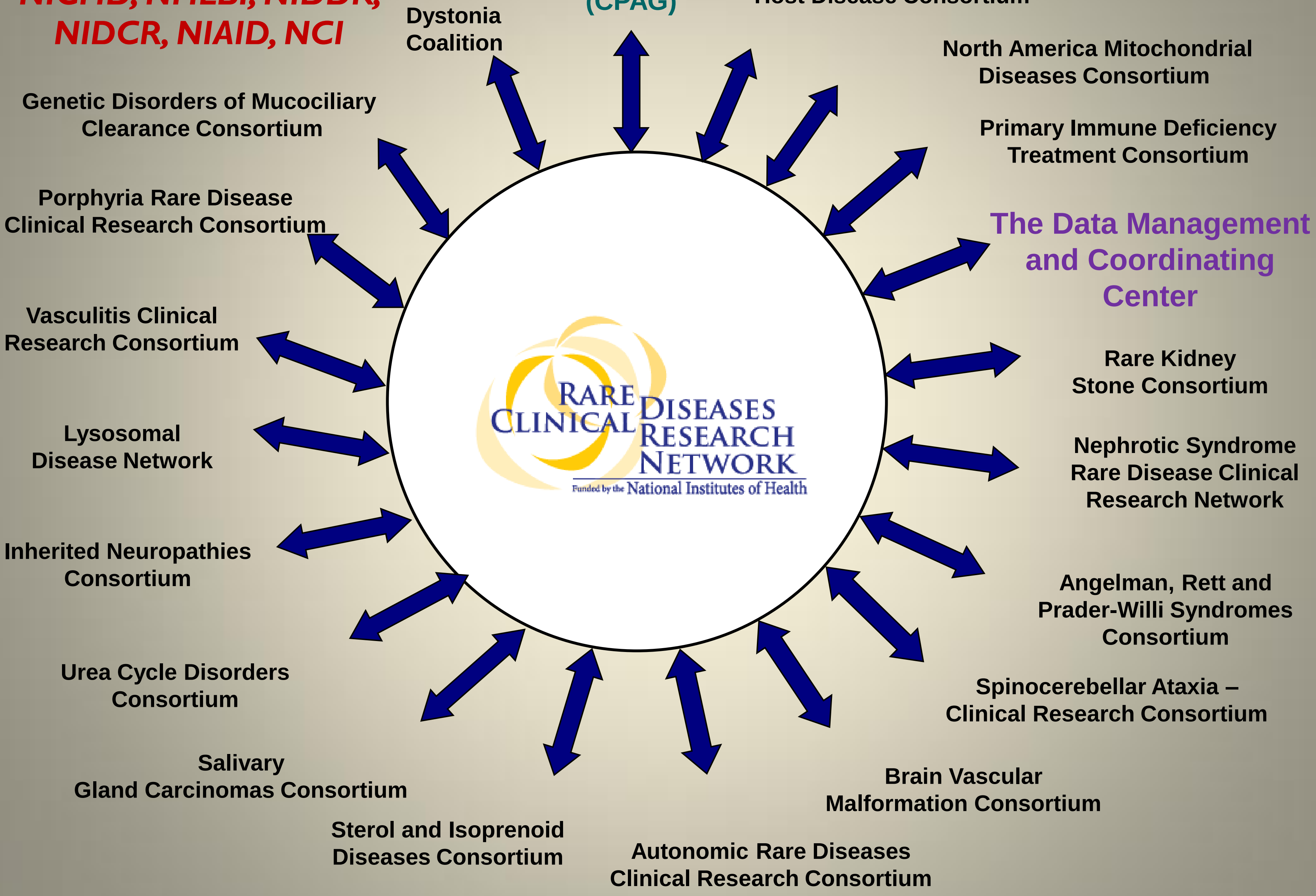
- Natural History Studies Workshop
  - Improve Understanding of Natural History of Rare Diseases
  - Improve Recruitment for Clinical Trials
  - Identify Possible Responders to Therapy More Effectively
  - Identify Clinical Endpoints and Develop Validated Biomarkers
  - Train Investigators with Appropriate Study Design
  - Identify Standards for Natural History Studies
  - NCATS - ORDR/DPI; FDA/CDER/OOPD; NIH/ICs
- https://www.team-share.net/Natural_History_Studies_Rare_Diseases/overview.aspx

RDCRN

- 18 Consortia with 225 institutions world-wide Studying >200 diseases
- More than 85 Patient Advocacy Groupss have formed Coalition of PAGs (CPAG)
- More than 100 New Investigators Trained Through Training Programs
- 83 protocols accruing patients Using Contact Registry
- ~ 14000 patients enrolled in studies (3000 recruited in 2012)
- Natural History Studies, Clinical Trials, Genotype/Phenotype

- URL: http://rarediseasesnetwork.epi.usf.edu/

DHHS-NIH
ORDR, NINDS, NIAMS, NICHD, NHLBI, NIDDK, NIDCR, NIAID, NCI



Coalition of Patient Advocacy Groups (CPAG)

Chronic Graft Versus Host Disease Consortium

North America Mitochondrial Diseases Consortium

Primary Immune Deficiency Treatment Consortium

The Data Management and Coordinating Center

Rare Kidney Stone Consortium

Nephrotic Syndrome Rare Disease Clinical Research Network

Angelman, Rett and Prader-Willi Syndromes Consortium

Spinocerebellar Ataxia – Clinical Research Consortium

Brain Vascular Malformation Consortium

Autonomic Rare Diseases Clinical Research Consortium

Sterol and Isoprenoid Diseases Consortium

Salivary Gland Carcinomas Consortium

Urea Cycle Disorders Consortium

Inherited Neuropathies Consortium

Lysosomal Disease Network

Vasculitis Clinical Research Consortium

Porphyria Rare Disease Clinical Research Consortium

Genetic Disorders of Mucociliary Clearance Consortium

Dystonia Coalition

Goals of RDCRN (Consortia and DMCC)

- Facilitate clinical research by:
  - Creating Consortia focused on related diseases
  - Cost-sharing research infrastructures
  - Establishing uniform protocols for data collection
  - Making meaningful collaborative clinical studies possible for longitudinal studies, pilot projects, and clinical trials
- Collaborate with Patient Advocacy Groups (PAGs) as research partners
- Train new investigators in rare diseases research
- Provide Website resource for education and research in rare diseases

Contact Information

Office of Rare Diseases Research, NIH
Phone: 301-402-4336
E-mail: ORDR@nih.gov
Web Site : http://rarediseases.info.nih.gov/

Genetic and Rare Diseases Information Center
Toll-free: 888-205-2311 TTY: 888-205-3223
E-mail: GARDinfo@nih.gov
Web site: http://rarediseases.info.nih.gov/GARD/

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- Ms. Henrietta Hyatt-Knorr
- Dr. Lata Nerurkar
- Ms. Susan Orr Lowe
- Ms. Geraldine Pollen
- Dr. William Gahl (Clinical Director, NHGRI)
- Dr. Yaffa Rubinstein
- Dr. P.J . Brooks (NIAAA)

Voice: 301-402-4336/ Fax: 301-480-9655

E-mail: ORDR@nih.gov http://rarediseases.info.nih.gov/

NIH…

Turning Discovery Into Health

Following slides for Information only

NIH-Industry Collaboration (Continued):

- **Pilot: 4-8, 2-3 year projects**
- **Request for applications and review process:**
  - **Pre-application based on limited information on the compounds**
  - **Successful applicants get more data on the compounds – submit full application**
- **MOU between NIH and Industry Partners**
- **Model template agreements are available**

- **NOT-TR-12-001**: Notice of Intent to Publish a Request for Pre-Applications for the NIH-Industry Pilot Program: Discovering New Therapeutic Uses for Existing Molecules (X02, UH2/UH3)
- **NOT-TR-12-002**: Request for Information: Input on the NIH-Industry Program, Discovering New Therapeutic Uses for Existing Molecules

Discovering New Therapeutic Uses for Existing Molecules

- PAR-12-203: A Pre-application for the NIH-Industry Pilot Program: Discovering New Therapeutic Uses for Existing Molecules (X02); http://grants.nih.gov/grants/guide/pa-files/PAR-12-203.html
- RFA-TR-12-004: Limited Competition for the NIH-Industry Pilot Program: Discovering New Therapeutic Uses for Existing Molecules (UH2/UH3); http://grants.nih.gov/grants/guide/rfa-files/RFA-TR-12-004.html
- RFA-TR-12-005: Limited Competition for the NIH-Industry Pilot Program: Discovering New Therapeutic Uses for Existing Molecules (UH3); http://grants.nih.gov/grants/guide/rfa-files/RFA-TR-12-005.html