

**I don't have any conflicts of interest**



# The NIH/NCATS GRDR<sup>®</sup> Program

A model to accelerate biomedical research  
in rare diseases:

*From a Concept to a Global Program*



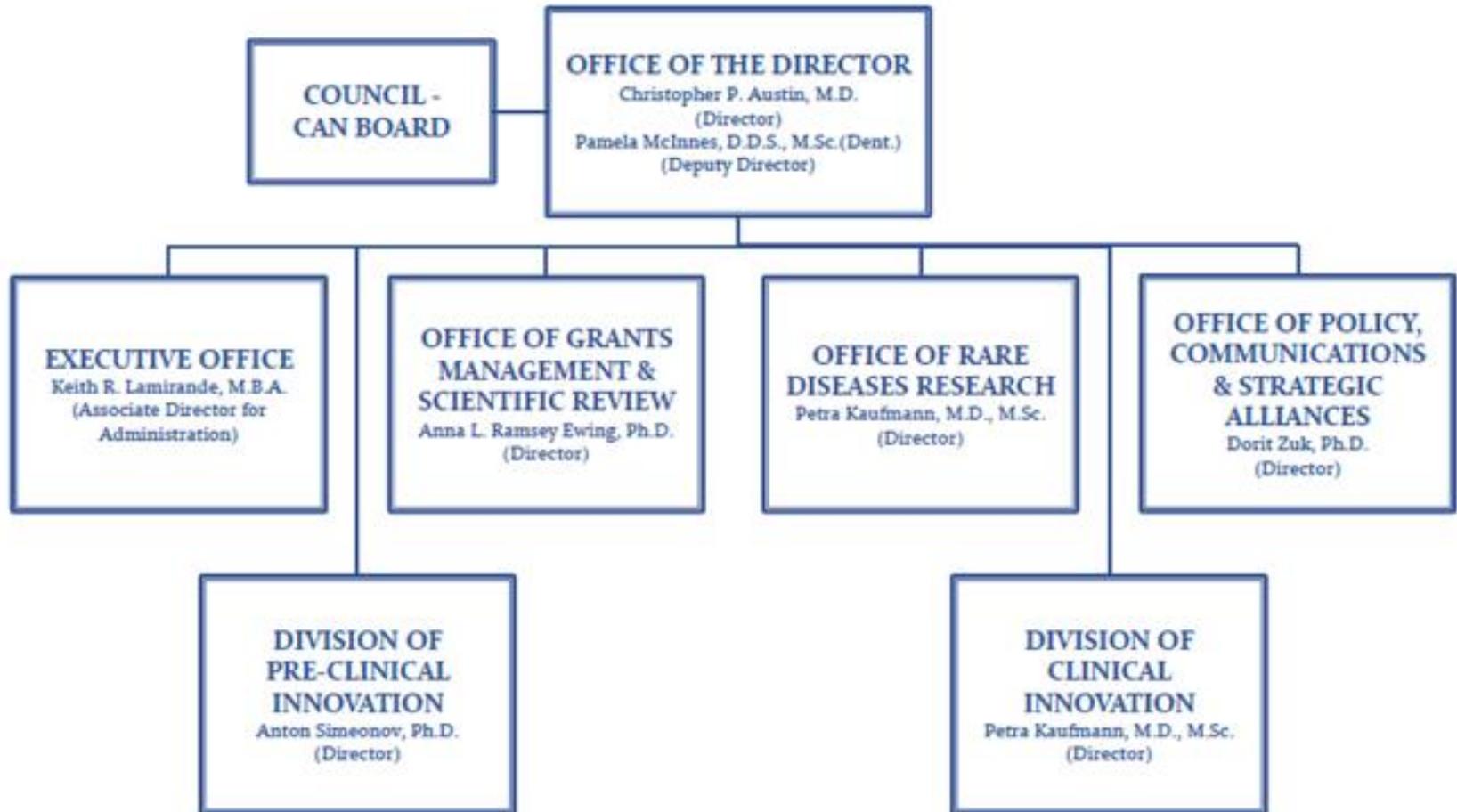
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National Center for Advancing Translational Sciences (NCATS)  
National Institutes of Health (NIH)

**ICORD, Mexico, 2015**



# NCATS Organizational Chart



# How to accelerate development of drugs and therapeutics for rare diseases?

Recognizing the needs and the issues, in 1983, Congress passed the Orphan Drug Act, to encourage research and drug development for rare diseases.

Before the law passed only 10 treatments were approved for rare diseases.

Since then, 494 treatment were approved.

**There are more than 6000 rare diseases;  
more progress is needed**

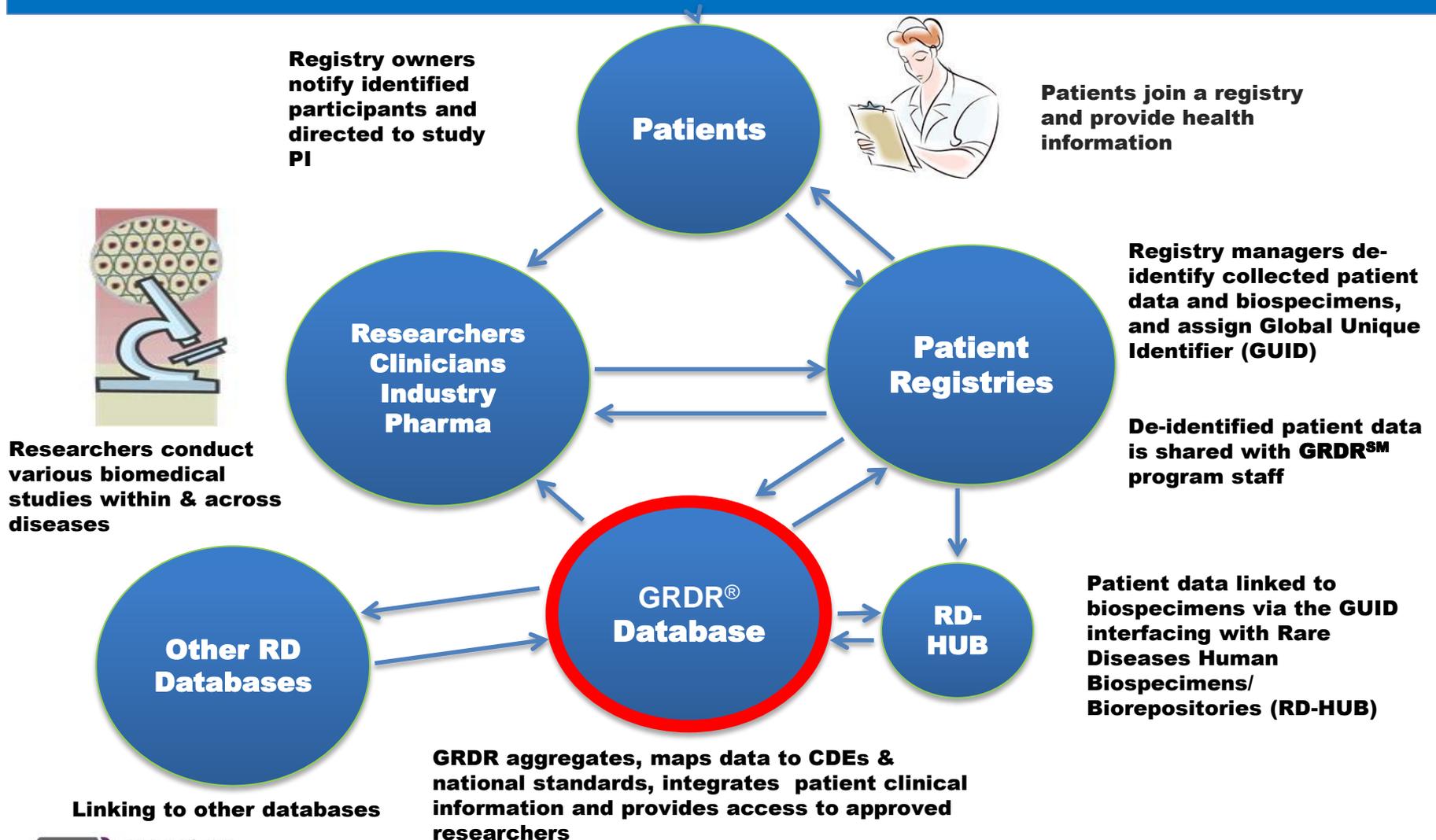


**Registries are an essential tool and an important resource for patients' data**



# GRDR® Data Repository

## Concept



# GRDR Common Data Elements

<https://ncats.nih.gov/grdr/cdes>

## Common Data Elements



- **Current contact information**
- **Socio-demographic information**
- **Diagnosis**
- **Family history**
- **Birth and reproductive history**
- **Anthropometric information**
- **Patient-reported outcome**
- **Medications/devices/health services**
- **Clinical research and biospecimen**
- **Communication preferences**

# Value of Common Data Elements

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Facilitate reproducibility of findings, and sharing and integrating data to have a better understanding of biological and clinical processes

<https://www.nlm.nih.gov/cde>

<https://cde.nlm.nih.gov/home>



# Value of sharing data

- Facilitates cross disease analyses
- Increases the statistical power and the scientific value by integrating data from multiple registries/studies into one database
- Facilitates reproducibility and validation of data collection and research results
- Facilitates development of novel treatments for patients, and tools for research



# Unique elements of GRDR data sharing

- Data mapped and integrated using national standards
- Each patient dataset is assigned a GUID
- No restriction on data sharing
- Patients agree to share data broadly for any approved research project
- Approval of research projects are based upon scientific merit of the proposed research



# NIH/NCATS/GRDR® Program Vision

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The NIH/NCATS Global Rare Diseases Patient Registry Data Repository/GRDR® program is designed to advance research for rare diseases and, through application of scientific insights gained, to further research for common diseases as well.



# NIH/NCATS GRDR® Program

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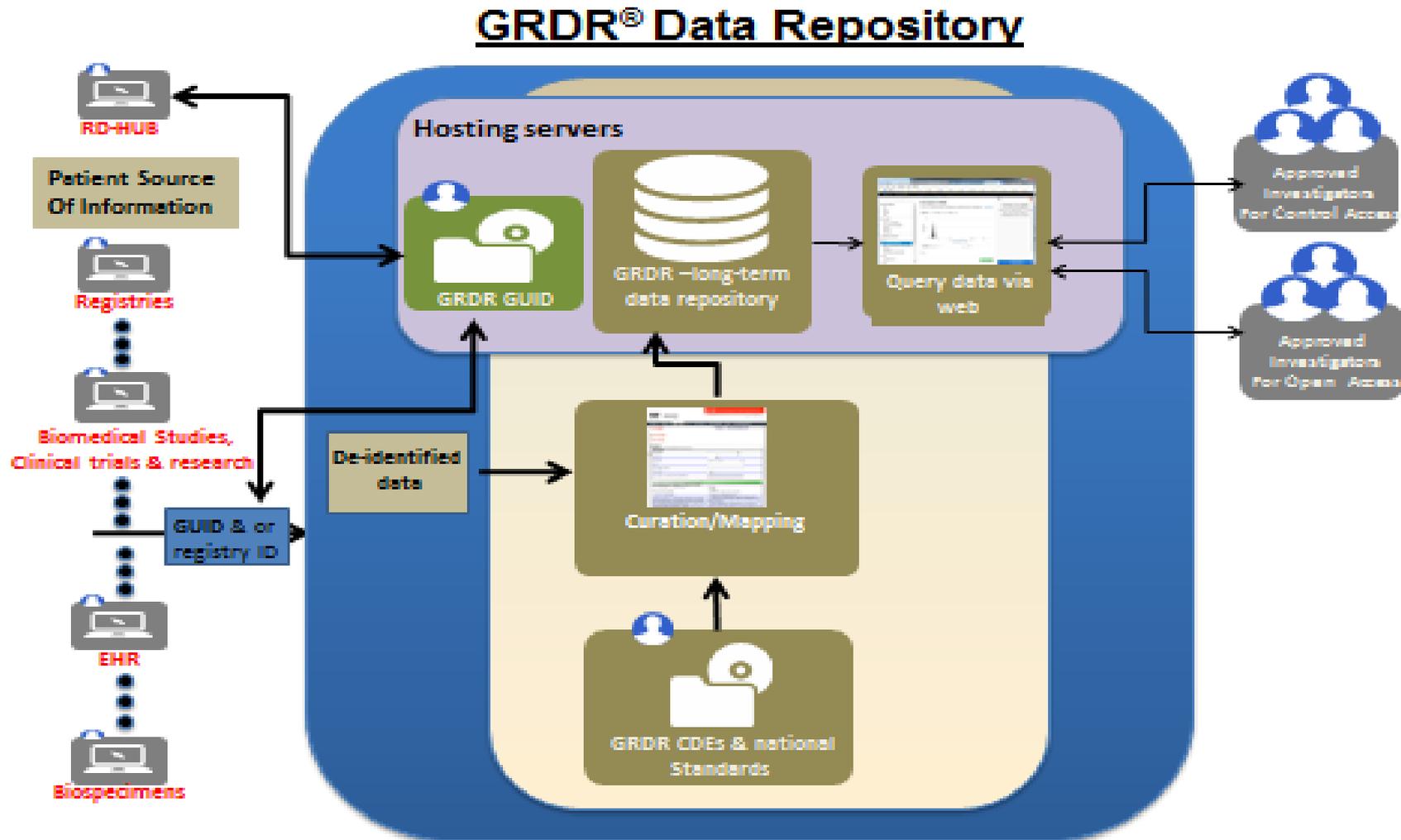
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- 1. Development, Engagement, Demonstration and Dissemination of Tools and Resources**
- 2. GRDR® Data Repository**



## 2. GRDR® Data Repository

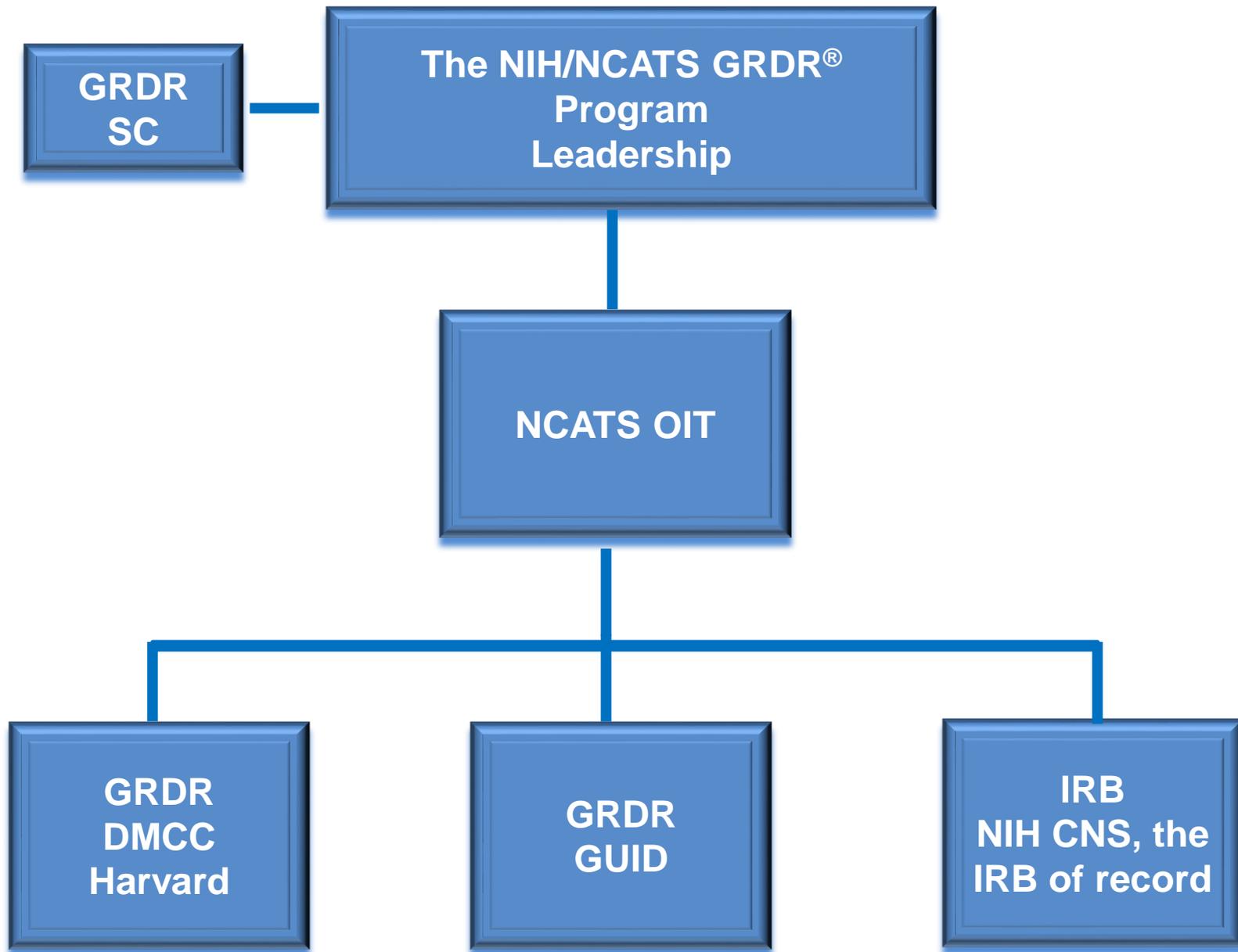
Developing a global web database of data patient information with rare diseases, and common diseases; integrating the data from patient registries, EHR and other data sources. The aim is to provide a resource for various biomedical studies including clinical trials.



# **The significance of bio-specimens and the linkage to patient clinical data**



# GRDR Program Organizational Chart



# The NIH/NCATS GRDR<sup>®</sup> Program Value

## For patients and their families:

- ❖ Increase awareness of their specific rare disease and facilitating accelerated therapeutic development.

## For physicians and nurses:

- ❖ Facilitate contact with others who are dealing with the same issues and compare notes.
- ❖ Provide access to outcomes data as a benchmark for their patients' progress.
- ❖ Provide awareness of treatment regimens that are being attempted and seek better outcomes for their patients through novel approaches.
- ❖ Provide access to treatment information so that the health care providers can see how often a treatment is used for the condition of their patient.
- ❖ Foster collaboration between physicians at medical centers, pharmaceutical industries, and patient advocacy groups



# The NIH/NCATS GRDR® Program Value continue

## For rare disease organizations:

- ❖ Provide resources and tools to establish a registry
- ❖ Map data from each registry to standards
- ❖ Facilitate interoperability among them and between other databases
- ❖ Create opportunities for collaboration and sustainability

## For investigators and industry:

- ❖ Allow free access to curated and standardized clinical and genomic data
- ❖ Provide a platform to set up multi-center clinical trials for rare diseases
- ❖ Facilitate research collaboration and cross-disease analyses by lowering barriers to data access



# The NIH/NCATS GRDR<sup>®</sup> Program Policies

- ❖ **Required elements for participation**
- ❖ **Data Submission Agreement**
- ❖ **Data Access Agreement**



# Examples of cross disease analyses and common pathways

## Collaboration between investigators studying human diseases in animal models to develop gene therapy to treat the diseases



Children born with X-linked myotubular myopathy, which affects about 1 in 50,000 male births, have very weak skeletal muscles, causing them to appear floppy. They also have severe respiratory difficulties. Survival beyond birth requires intensive support, often including tube feeding and mechanical ventilation, but effective therapy is not available for patients, and most die in childhood. using an engineered adenovirus vector, vector carries a replacement *MTM1* gene used in two animal models: mice and dogs. Both animals responded to a single intravascular injection of an adenovirus vector engineered for gene replacement therapy.

# Examples of cross disease analyses and common pathways

**Targeting same mutation in two different diseases:** mutated ryanodine receptor type 1 (RyR1) in Malignant hyperthermia (MH) and in myotubular myopathy

**Increasing the statistical power by increasing the sample size (data):**

heritable disorders linked by intolerance of the body to glucose: Bardet–Biedl, Wolfarm and WABB



# Faces of the children



# Faces of the children



# Success metrics of the GRDR Program



# NCATS Newsletter release Sept. 23, 2015



## NCATS and Harvard Collaborate to Advance Global Rare Diseases Data Repository

The NIH/NCATS Global Rare Diseases Patient Registry Data Repository/GRDR® program is designed to advance research on rare diseases and, through application of scientific insights gained, to further research on common diseases as well. The goal is to develop a Web-based resource that integrates, secures and stores many different types of de-identified patient information from a wide range of sources — registries, electronic health records, research datasets, biospecimen repositories and more —all in one place.

The ability to retrieve data from such varied sources will enable researchers to conduct comparative and cross-disease analyses. Combining data from many disorders and facilitating its use in state-of-the-art collaborative research ultimately may lead to new understanding of these illnesses as well as the development of new drugs and therapeutics for the millions of patients with rare diseases.

In August 2015, NCATS awarded a supplemental grant to the Harvard Medical School (HMS) Department of Biomedical Informatics (DBMI) to further develop the GRDR. Led by Isaac Kohane, M.D., Ph.D., and Paul Avillach, M.D., Ph.D., the DBMI efforts will build in part on [NIH's Big Data to Knowledge](#) and related initiatives.

This NCATS-HMS collaboration will enable work to integrate different patient registries into the GRDR program and provide secure, encrypted access to these data to authorized users. Using this approach, data providers can more easily share their data with the wider research community and ultimately help get more treatments to more patients more quickly. Learn more about [NCATS' GRDR program](#) and [Harvard's DBMI](#).





## News

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### DBMI and NCATS to Collaborate on Global Rare Diseases Data Repository

September 28, 2015



Image courtesy of NCATS

In August 2015, the National Center for Advancing Translational Sciences (NCATS) awarded DBMI a supplemental grant of \$2.4M to further develop the **Global Rare Diseases Patient Registry Data Repository/GRDR®** program. Led by Isaac Kohane, M.D., Ph.D., and Paul Avillach, M.D., Ph.D., the efforts will build in part on DBMI's **PIC-SURE** platform (Patient-Centered Information Commons: Standardized Unification of Research Elements), which is a project based on the **i2b2** and **tranSMART** platforms and funded by **NIH's Big Data to Knowledge (BD2K)** initiative.

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