



# FOCUS ON RARE DISEASES



THE OFFICE OF RARE DISEASES RESEARCH NEWSLETTER  
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## *Highlights of the Office of Rare Diseases Research Activities*

### *Rare Diseases Clinical Research Network (RDCRN II) Update*

In the fall of 2009 the NIH Office of Rare Diseases Research (ORDR) in collaboration with seven NIH Institutes (NICHD, NHLBI, NIDDK, NIAMS, NINDS, NIDCR, and NIAID) renewed and expanded the RDCRN Program. The level of support received from the ICs (institutes and centers) has increased, and in the expanded RDCRN (called RDCRN II) ORDR was able to provide support for 19 consortia. The Data and Technology Coordinating Center has been continued in RDCRN II as the Data Management Coordinating Center with a slightly different charge. In RDCRN II, 56 Patient Advocacy Groups (PAGs) are participating and collaborating in the clinical studies of more than 90 rare diseases at over 130 research sites. The first Steering Committee and Orientation Meeting for the Principal Investigators (PIs) was held on October 1-2, 2009. This meeting was also attended by PAGs, co-PIs, and relevant program staff from the ICs.

Below is a link to the NIH press release about the expansion of Rare Diseases Clinical Research Network.  
<http://www.nih.gov/news/health/oct2009/od-05.htm>

### *Collaboration, Education, and Test Translation Program for Rare Genetic Diseases (CETT)*

People affected by rare inherited diseases need the reliable information that comes through quality genetic testing. The goal of the CETT Pilot Program is to help facilitate the translation of new tests for rare genetic diseases. The program's objectives are to translate as many appropriate tests as possible, ensure that the best possible test is offered in light of current knowledge, and ensure that the test meets the needs of the community. All tests are important whether the specific condition affects 5 people or 50,000.

The CETT Pilot Program's objectives require a strong collaboration between researchers, clinicians, patient advocates and clinical laboratories. The program has several new enhancements to facilitate the development of collaborations, researcher consultation, and educational materials. The program also supports the electronic collection of genetic and clinical data in public databases to accelerate access to the information for new research and treatment possibilities.

Discussions are underway to determine the future function of this pilot program and how to move it to permanent status within the NIH to best serve the public. For more information, please visit: <http://rarediseases.info.nih.gov/cettprogram/about.aspx>

### ***NIH Undiagnosed Diseases Program***

The National Institutes of Health (NIH) launched the Undiagnosed Disease Program (UDP) in May of 2008 to evaluate patients with disorders that have evaded a diagnosis. Often such patients, seek help from multiple physicians and other health care providers over many years before a diagnosis is made. The UDP has been organized by the National Human Genome Research Institute (NHGRI), the Office of Rare Diseases Research (ORDR), and the NIH Clinical Center. The program's main goals are to provide answers to patients with mysterious conditions that have long eluded a diagnosis and to advance medical knowledge about rare and common diseases.

By all accounts, the program has been successful. More personnel have been hired and funding has been increased. Over the year and a half since its inception, there have been more than 3000 inquiries, more than 1200 medical records submitted, 300 patients accepted, and about 220 of these patients seen so far at the NIH Clinical Center in Bethesda, MD. It is interesting that over half of the applications fall into the realm of neurology. As an indication of the seriousness of the illnesses for which patients are applying, thirteen who have applied have died, most before they could be seen at the Clinical Center. There have been five to ten true diagnoses made. In one of these, a family with arterial calcifications of the lower extremities, a causative mutation was found in a gene not known to be involved in any other disease. The UDP provides both diagnostic support and new insights into rare diseases.

Additional information can be found at: <http://rarediseases.info.nih.gov/Resources.aspx?PageID=31>

### ***Therapeutics for Rare and Neglected Diseases (TRND) Program***

Both the need and opportunity for Therapeutics for Rare and Neglected Diseases (TRND) are enormous. Of the 7,000 human diseases, fewer than 300 are of interest to the biopharmaceutical industry, due to limited prevalence and/or commercial potential. More than 6,000 of these diseases are rare (defined by the Orphan Drug Act as <200,000 U.S. prevalence), and the remainder are neglected because they affect impoverished or disenfranchised populations. Researchers have now defined the genetic basis of more than 2,000 rare diseases and identified potential drug targets for many rare and neglected diseases (RND).

TRND received \$24 million in the NIH budget for fiscal year 2009. TRND is a collaborative drug discovery and development program with governance and oversight provided by Office of Rare Diseases Research. Program operations will be within the intramural research program administered by the [National Human Genome Research Institute](#).

For more information, please see the Program to Advance Development of Drug Candidates for Rare and Neglected Diseases Request for Information (RFI) webpage:

<https://www.fbo.gov/spg/HHS/NIH/NHLBI/NHLBI-NHGRI-2010-112/listing.html>

### ***Creating a Global Rare Disease Registry***

In January 2010, the Office of Rare Diseases Research (ORDR) organized a workshop, *Advancing Rare Disease Research: The Intersection of Patient Registries, Biospecimen Repositories, and Clinical Data*, to discuss the development of an infrastructure for an internet-based rare disease patient registry, which would also include access to biospecimens. The workshop was sponsored by ORDR and the National Eye Institute (NEI), the National Center for Research Resources (NCRR), patient advocacy groups, and the private sector. Workshop attendees discussed approaches to creating a federated registry that would collect and aggregate patient data, serve as a core data repository and also link to other existing registries. This would allow expanded data access for patients, families, clinicians and researchers seeking accurate information. As an additional aid to research, the registry would also link to biorepositories of rare disease biospecimens.

During the presentations and breakout sessions, attendees representing advocacy groups, researchers, information technology experts, and government and private sector personnel dealt with issues related to this umbrella infrastructure. Workshop attendees expressed an enthusiasm and a commitment to getting involved and making it happen. Post workshop committees will guide the effort as it moves forward.

### ***NIH Announces Genetic Testing Registry***

The NIH announced on March 18 that it is creating a public database that researchers, consumers, health care providers, and others can search for information submitted voluntarily by genetic test providers. The Genetic Testing Registry aims to enhance access to information about the availability, validity, and usefulness of genetic tests. For more information please see:

<http://www.nih.gov/news/health/mar2010/od-18.htm>

### ***NIH Biospecimen Interest Group***

On Thursday, April 15, 2010, the NIH Biospecimen Interest Group (BIG) held a meeting that featured a series of presentations on biospecimen resources within and supported by the NIH. BIG is sponsored by the Office of Rare Diseases Research and the Office of Biorepositories and Biospecimen Research, National Cancer Institute (OBBR/NCI).

The event, which took place in the Masur Auditorium in the Clinical Center, was well attended, and the attendees found it very informative. The interest group offers a forum for trans-NIH interactions and enhanced information sharing. Members were asked to share ideas for future meetings.

The meeting included the following presentations:

- “The NIDDK Central Repositories”
- “eyeGENE (NEI) Genotype/Phenotype Database, Repository and Registry”
- “Tissue Biospecimens in Cancer Epidemiology Studies”

“The National Cancer Institute's Cooperative Human Tissue Network”  
“BioLINCC: Access to NHLBI Biospecimens and Data”

The event was videocast and is available for viewing. (<http://videocast.nih.gov/summary.asp?live=8662>)

### ***VI International Conference on Rare Diseases and Orphan Drugs in Buenos Aires (ICORD 2010)***

A global meeting on international cooperation and policies for rare diseases and orphan products was held in Buenos Aires, Argentina on March 18-20, 2010. *The VI International Conference on Rare Diseases and Orphan Drugs (ICORD 2010)* convened for the first time in the southern hemisphere in agreement with its aim of globalization of rare diseases research and orphan products development activities.

Individuals and organizations from patient groups, academic research investigators, the pharmaceutical, biotechnology and medical device industries, and government policy and decision makers were invited to participate in this unique forum. Specialized courses, and open meetings with key people in the field were available for participation during the days previous to the conference (March 16 and 17), as well as a pre-meeting about the Latin American and Caribbean initiatives (ER2010LA) in rare diseases and orphan products.

Because of its nature, rare diseases would be better researched and managed within an international landscape, and this conference offered the opportunity to join the discussion of the ideas and global needs of the rare diseases community. The economic impact of introducing new therapies and how cooperative strategies may influence the cost of these treatments was a special topic along with the special informational and individual needs of the patients and families across the lifespan. Also of interest were the particular needs of the developing world in the management of diseases that are rare in developed countries but neglected in the environments where the diseases occur more frequently

GEISER Foundation, the first non-profit umbrella organization for rare diseases in Latin America and the Caribbean hosted the conference and the pre-activities. Information about the conference is found on the [ICORD 2010 conference website](#). (Presentations will be available later on [www.icord.se](http://www.icord.se)).  
GEISER Foundation on the web: <http://www.fundaciongeiser.org>

### ***International Collaborations: Japan and Korea***

The Office of Rare Diseases Research held two meetings in early 2010 with overseas visitors interested in rare diseases research and orphan products development. The first meeting took place in January with visiting scientists from the Japanese Ministry of Health, Labour and Welfare and the National Institute of Public Health. The second meeting was held in February with scientists from the Korean National Institute of Health, Sungkyunkwan University and Seoul National University.

The NIH agenda topics included:

- Genetic and Rare Diseases Information Center (ORDR)
- Undiagnosed Diseases Program (NIH: ORDR, Clinical Center, Institutes)
- Clinical Trials.gov (NIH)
- Therapeutics for Rare and Neglected Diseases Program (NHGRI)
- Rare Diseases Clinical Research Network (ORDR, Institutes)
- Genetic Test Translation Program (CETT/ORDR)
- Clinical Center programs and protocols

- Clinical and Translational Science Awards, Clinical Research Network Program (NCRR)
- Office of Orphan Product Development (FDA)

Presentations were also made by the Japanese and Korean visitors describing their health and research organizations, and their research and product development activities. The meeting agendas allowed ample opportunity for discussion following each talk. ORDR also included a presentation on an educational module on rare diseases designed for middle school students, which when completed, will be available at no expense not only in the United States but also to other countries for their use.

The NIH and other US presenters and the Japanese and Korean presenters agreed that their meeting was successful in advancing communication, sharing knowledge, and stimulating potential research collaborations in rare diseases research and orphan products development.

### ***Science of Small Clinical Trials Course***

"The Science of Small Clinical Trials," a course created jointly by the FDA's [Office of Orphan Products Development](#) (OOPD) and NIH's [Office of Rare Diseases Research](#), , deals with issues concerning the design and analysis of clinical trials based on small study populations. While small clinical trials are a necessity in the context of rare diseases, being able to conduct small trials with scientific rigor is of increasing importance in other contexts, particularly as genomic science begins to provide opportunities for individualized pharmacology. Over 1500 individuals requested for the course.

<http://small-trials.keenminds.org/>

<http://videocast.nih.gov/PastEvents.asp?c=88>

### ***Rare Cancers with High Mortality: Challenges for Cancer Prevention and Treatment***

Recently a workshop, *Rare Cancers with High Mortality: Challenges for Cancer Prevention and Treatment*, was held to discuss the issues and challenges associated with rare cancers and to facilitate collaborations among the participants. Approximately 200 participants including scientists, clinicians, industry, government, and patient advocates met for the workshop.

The day and a half workshop was structured with plenary sessions for the first half-day followed by three Breakout Groups for facilitating discussions among the participants. The Breakout Groups were divided into the following areas: (A) Building a Knowledge Base – Biology, Epidemiology, and Etiology; (B) Facilitating Clinical Studies in Rare Cancers; and (C) Development of New Detection, Prevention Methods/Strategies, and Therapies. On the second day, the moderators of each Breakout Groups presented a summary for discussion to all participants.

All three Breakout Groups identified similar issues and challenges in the study of rare cancers and common themes for addressing these challenges. This report outlines the outcome of this workshop and the recommendations provided by the participants of this workshop:

[http://rarediseases.info.nih.gov/RARE\\_CANCERS\\_WORKSHOP/](http://rarediseases.info.nih.gov/RARE_CANCERS_WORKSHOP/)

### ***Research Challenges in CNS Manifestations of Inborn Errors of Metabolism Workshop***

On December 7 and 8, 2009, the Office of Rare Diseases Research, the National Institute of Neurological Disorders and Stroke and the Food and Drug Administration's Center for Drug Evaluation and Research, Division of Gastroenterology Products, hosted a workshop on the central nervous system (CNS) and inborn errors of metabolism, *Research Challenges in CNS Manifestations of Inborn Errors of Metabolism*. More than 150 participants attended the meeting to discuss the barriers to the development of therapies for central nervous system disease in inborn errors of metabolism (IEM). The conference focused on the challenges in clinical translation including the regulatory requirements to move from preclinical to the clinical stage of research and development, consideration of specific clinical trial design for rare diseases, the identification of appropriate outcome measures for evaluation of interventions, and ethical issues related to the investigation of products for these diseases.

Additional meeting information can be found at:

[http://www.rarediseases.info.nih.gov/Inborn\\_Errors\\_Metabolism/AddContact.aspx](http://www.rarediseases.info.nih.gov/Inborn_Errors_Metabolism/AddContact.aspx)

### ***Opsoclonus Myoclonus Syndrome (OMS) Workshop***

The *Opsoclonus Myoclonus Syndrome (OMS) Workshop* was held on April 10, 2010 at the Westin Harbour Castle in Toronto, Canada. Approximately 35 researchers, patient advocates, and industry representatives from 7 countries met along with several NIH representatives to discuss issues of importance to the OMS community, including the differences between pediatric OMS and adult onset OMS, therapeutic strategies in the US and Europe, diagnostic criteria, current research activity and future directions. It was felt that there was enough agreement in several areas that consensus documents could be drafted. It is hoped that another OMS conference can be scheduled in approximately a year both to leverage the momentum from the first meeting into real collaborative progress in the OMS community and to fit better with the biennial meetings held in Europe.

[http://rarediseases.info.nih.gov/oms\\_workshop/](http://rarediseases.info.nih.gov/oms_workshop/)

### ***ORDR Scientific Conference Program***

ORDR collaborates with Institutes, Centers, and Offices at NIH to stimulate rare diseases research by cosponsoring scientific conferences where research is lagging or to take advantage of scientific opportunities. In 2009, ORDR co-supported over 90 conferences. This year, ORDR will co-support up to 50 conferences.

Since the program inception in 1995 ORDR has co-supported almost 1100 conferences. For more information please visit [http://rarediseases.info.nih.gov/Scientific\\_Conferences.aspx](http://rarediseases.info.nih.gov/Scientific_Conferences.aspx)

## ***About ORDR***

The Office of Rare Diseases Research (ORDR) was established in 1993 within the Office of the Director of the NIH, the Nation's medical research agency. Public Law 107-280, the [Rare Diseases Act of 2002](#), established the office in statute. The goals of ORDR are to stimulate and coordinate research on rare diseases and to respond to the needs of patients who have any one of the almost 7,000 rare diseases known today.

Definition of rare diseases: (Orphan Drug Act as amended in 1984 by P.L. 98-551 to add a numeric prevalence threshold to the definition of rare diseases.)

*“...the term, rare disease or condition means any disease or condition which (a) affects less than 200,000 persons in the U. S. or (b) affects more than 200,000 persons in the U.S. but for which there is no reasonable expectation that the cost of developing and making available in the U. S. a drug for such disease or condition will be recovered from sales in the U. S. of such drug.”*

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