

TESTIMONY SUBMITTED FOR RECORD

To The

**HOUSE APPROPRIATIONS SUBCOMMITTEE ON AGRICULTURE,
RURAL DEVELOPMENT, FOOD AND DRUG ADMINISTRATION
AND RELATED AGENCIES**

By The

**NATIONAL ORGANIZATION FOR RARE DISORDERS (NORD)
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Regarding

**FY 2003 APPROPRIATIONS FOR THE
ORPHAN PRODUCTS RESEARCH GRANT PROGRAM
AT THE
FOOD AND DRUG ADMINISTRATION (FDA)**

National Organization for Rare Disorders
Testimony Submitted for the Record Regarding
FY 2003 Funding for the Orphan Product Research Grant Program
March 2002

Mr. Chairman and members of the House Appropriations Subcommittee on Agriculture, Rural Development, Food and Drug Administration and Related Agencies, the National Organization for Rare Disorders (NORD) wishes to express its views regarding appropriations for the Orphan Products Research Grant Program administered by the Office of Orphan Product Development (OOPD) at the Food and Drug Administration (FDA).

NORD is a federation of approximately 140 voluntary health organizations and over 70,000 individual patients, healthcare providers and clinical researchers dedicated to helping the 25 million people in the United States suffering with rare “orphan” diseases. An orphan disease is defined by statute as any disease or condition impacting fewer than 200,000 Americans (The Orphan Drug Act of 1983). It makes no difference whether you are male or female, rich or poor, young or old, white, African-American, Latino, Asian or American Indian. These diseases affect everyone.

In 1989 the HHS *National Commission on Orphan Diseases* estimated that only 30 percent of the 25 million patients suffering with rare diseases receive a diagnosis in three to five years after the onset of symptoms. That works out to about 7.5 million patients who are shuffled from specialist to specialist, year after year. Fifteen percent, or 3.7 million people, wait seven years or more. And even after diagnosis, they can only hope that someone, somewhere, will conduct research to develop a treatment for their disease.

Recognizing that the rare disease community has not received sufficient funding, Senators Edward Kennedy and Orrin Hatch introduced the Rare Diseases Act of 2001, S. 1379, on August 3, 2001. This important legislation would provide additional funding for the Orphan Product Research Grant Program at the FDA in the amount of \$25 million.

On March 20, 2002, Mr. Mark Foley and Mr. Henry Waxman introduced the **Rare Diseases Orphan Product Development Act of 2002, H.R. 4014**, which would increase funding to \$25 million for the Food and Drug Administration’s *Orphan Product Research Grants Program*.

Note: The **Rare Diseases Act of 2002, H.R. 4013**, was also introduced on March 20, 2002, by Mr. John Shimkus and Mr. Henry Waxman and would provide for the statutory authorization for the existing *Office of Rare Diseases* (ORD) at the National Institutes of Health (NIH) in order to enhance the national investment in the development of diagnostics and treatments for patients with rare disorders. Additional funding for the office will augment NIH Institutes’ research for neglected rare diseases in order to take advantage of emerging research opportunities.

On behalf of the 25 million Americans suffering with the over 6,000 known rare “orphan” diseases and the 119 organizations currently advocating for increased funding for this worthy program, we respectfully request that this Subcommittee support H.R. 4014 and appropriate the necessary funding authorized by this legislation. Just one dollar for each and every person suffering with a rare disease appropriated for the FDA’S Orphan Products Research Grant Program represents a minimal investment by the federal government in the development of lifesaving treatments in which the private sector has no interest. But the return on investment could be phenomenal if only a few new orphan drugs or devices are developed to reduce the burden of disease and death for thousands of patients with rare disorders.

Appropriating just one dollar for each rare disease patient in America, rather than the current funding level, is a win-win proposition. Patients win when their symptoms are alleviated or cured. Families win when their loved ones no longer suffer. Society, as a whole, wins when patients are able to return to school or work to become productive tax-paying citizens. Pharmaceutical and biotechnology companies win when they are able to market new therapeutic products when part of the development costs are subsidized. The scientific community wins when the knowledge it gains can be applied to more prevalent diseases. And, finally, the government wins when the drain on healthcare dollars is minimized.

FDA Orphan Products Research Grant Program

This Subcommittee created the research grant program in FY 1983 to provide funding for pivotal clinical trials on new orphan drugs, medical devices, and medical foods for rare diseases. The funds have been made available to academic scientists and small companies. By definition, “orphan products” are treatments for rare conditions that have small potential markets and thus are not attractive to the commercial sector. Such treatments were not being developed for “orphan” diseases by the private sector until the *Orphan Drug Act* was enacted in 1983.

Since then, the FDA has approved 227 orphan drugs for marketing, and more than 800 additional drugs are in the research pipeline. Of those products approved for marketing, 27 (23 drugs and 4 medical devices) were developed with funding from the orphan product grants. **These 27 treatments would not be on the American market today saving the lives of thousands of Americans, enabling them to return to school or work, if this Subcommittee had not created this small but critically important pool of research funds.**

Most of FDA’S Orphan Products Research Grants support small clinical trials at academic institutions throughout the nation to develop the preliminary evidence that is necessary to attract commercial sponsors. It is the quintessential model for a successful government/industry partnership. There is no more appropriate program deserving of federal support because it fills a major gap between academic research and the private sector, and it creates lifesaving products that are needed throughout the world.

For example, children with Severe Combined Immune Deficiency (“Bubble Boy Disease”) no longer have to live in a plastic bubble because now their immune systems can fight off germs, thanks to an orphan drug developed with these grant funds. Children with urea cycle disorders no longer slip into a coma and die because an orphan drug enables their bodies to eliminate toxic

levels of ammonia. Babies born without ribs no longer suffocate in infancy because an artificial rib (orphan medical device) is being developed now with funds from the Orphan Products Research Grant Program that allows the children's lungs to expand and breathe. Cystic fibrosis, Crohn's disease, and multiple sclerosis drugs are on the market today only because these grants supported some of their research.

Unfortunately, there are many diseases and conditions that are simply too rare to attract private investment because the commercial sector is not interested in developing treatments for small markets. The investment necessary for research and development of new drugs and devices is too large in comparison to the size of the potential market for a rare disease. Case in point, there are only about 125 patients in the United States suffering with an orphan disease called fibrodysplasia ossificans progressiva (FOP), only 15,000 with Huntington's disease, and only 30,000 with cystic fibrosis. Many of the genetic diseases each impact no more than 40,000 Americans, whereas drugs for cancer, arthritis and hypertension each affect many millions of Americans, representing several billion dollars in potential sales each year.

Given the fact that the Orphan Products Research Grant Program is attracting greater attention, more researchers are eager to participate each year. Therefore, it is very unfortunate that the annual appropriation for this program cannot begin to cover all of the meritorious grant requests for promising research projects. About 100 grant applications are received annually, but many scientifically important applications are never funded simply because the appropriation is too small to meet the needs of the program. In fact, the appropriation now is less than it was in FY 1995, and has remained between \$10 to \$12 million for many years.

Mr. Chairman, if the government does not fund this research, who will? The private sector is simply not interested in rare diseases. If this Subcommittee does not meet the need of this unique sector of scientific research, people with rare diseases will be further victimized by the injustice of the supply and demand marketplace. For these diseases, no company wants to supply a treatment when the market demand is small.

Conclusion

And so, on behalf of the medically disenfranchised Americans and their families, we respectfully request that the members of this Subcommittee appropriate no less than \$25 million to the FDA Orphan Products Research Grant Program for FY 2002. We are relying on the members of this Subcommittee to fill the void between government and the private sector, and propel these treatments forward from academic laboratories to our local pharmacies. Ultimately, your compassion and insight will put new orphan drugs and devices into the waiting hands of critically ill patients. If you don't provide adequate resources for the Orphan Products Research Grant Program, unfortunately no one else will.

For additional information about the Rare Diseases Act of 2001, S. 1379, please contact Diane E. Dorman, Vice President for Public Policy, (202) 496-1296 or via e-mail at ddorman@rarediseases.org.

Thank you.

Attachment I
Supporting Organizations

Alpha-1 Association, Minneapolis, MN
Alpha-1 Foundation, Miami, FL
Alpha1VOICE, Evansville, IN
Alstrom Syndrome International, Mount Desert, ME
American Brain Tumor Association, Des Plaines, IL
American Hemochromatosis Society, Lake Mary, FL
American Laryngeal Papilloma Foundation, Spring Hill, FL
American Syringomyelia Alliance Project (ASAP), Longview, TX
Angel Flight America, Virginia Beach, VA
Angel Flight Samaritans, Fairfax, VA
Angel Flight for Veterans, Fairfax, VA
ARPKD/CHF Alliance (Autosomal Recessive Polycystic Kidney Disease & Congenital Hepatic Fibrosis),
Kirkwood, PA
Association of Glycogen Storage Disease (U.S.), Durant IA
Barth Syndrome Foundation, Perry, FL
Batten Disease Support and Research Association, Reynoldsburg, OH
Biotechnology Industry Organization (BIO), Washington, DC
Blepharophimosis, Ptosis, Epicanthus Inversus (BPEI) Family Network, Pullman, WA
Cardio-Facio-Cutaneous Family Network, Vestal, NY
CARES (Congenital Adrenal Hyperplasia Research, Education & Support) Foundation, Short Hills, NJ
Carol Ann Foundation, The, Tucson, AZ
Celgene Corporation, Chevy Chase, MD
Children's Angel Flight, Virginia Beach, VA
Children's Brittle Bone Foundation, Pleasant Prairie, WI
CDG Family Network Foundation, The, Shannon, IL
Chromosome 9p- Network, Las Vegas, NV
Chronic Granulomatous Disease Family Network Foundation
Coalition of Advocates for Research on the Eye (CARE), Sharon, MA
Coalition of Heritable Disorders of Connective Tissue, Sharon, MA
Cornelia de Lange Syndrome (CdLS) Foundation, Avon, CT
Corticobasal Ganglionic Degeneration (CBDG) Support Group, Haslett, MI
Cystinosis Foundation, Oakland, CA
Cystinosis Research Network, Burlington, MA
Dubowitz Syndrome Information & Parent Support, Visalia, CA
Dystonia Medical Research Foundation, Chicago, IL
Ehlers-Danlos National Foundation, Los Angeles, CA
Fabry Support & Information Group, Concordia, MO
Families of Spinal Muscular Atrophy (SMA), Libertyville, IL
FOD (Fatty Oxidation Disorder) Family Support Group, Greensboro, NC
FORCE: Facing Our Risk of Cancer Empowered, Coral Springs, FL
Foundation for Ichthyosis & Related Skin Types, Lansdale, PA
Genetic Alliance, Washington, DC
Genetics Information and Patient Services, Phoenix, AZ
Hallervorden-Spatz Syndrome Association, El Cajon, CA
Hermansky-Pudlak Syndrome (HPS), Oyster Bay, NY
Hydrocephalus Association, San Francisco, CA
Immune Deficiency Foundation, Towson, MD
Incontinentia Pigmenti International Foundation, New York, NY

International Children's Anophthalmia Network (ICAN), Philadelphia, PA
International Joseph Disease Foundation, Livermore, CA
International Morquio Support Group, Tucson, AZ
International Rett Syndrome Association, Clinton, MD
International Society for Mannosidosis & Related Diseases, Baltimore, MD
Interstitial Cystitis Association, Rockville, MD
Joubert Syndrome Foundation, Baltimore, MD
Kennedy's Disease Association, Simi Valley, CA
Kids With Heart National Association for Children's Heart Disorders, Green Bay, WI
Klinefelter Syndrome and Associates, Roseville, CA
LAM (Lymphangiomyomatosis) Foundation, Cincinnati, OH
Les Turner ALS Foundation, Skokie, IL
Lewy Body Disease Association, The, Brooklyn, NY
Lowe Syndrome Association, West Lafayette, IN
MAGIC Foundation, The, Oak Park, IL
Mannosidosis and Related Diseases, The International Society for, Baltimore, MD
Medical Journeys Network, Alexandria, VA
Mercy Medical Airlift, Virginia Beach, VA
Mastocytosis Society, Spanish Fork, UT
National Coalition for PKU & Allied Disorders, Mansfield, MA
National Foundation for Ectodermal Dysplasias, Mascoutah, IL
National Hemophilia Foundation, New York, NY
National Incontinentia Pigmenti Foundation, New York, NY
National Marfan Foundation, Port Washington, NY
National MPS (Mucopolysaccharidoses/Mucopolysaccharidoses) Society, Downingtown, PA
National Multiple Sclerosis Society, Washington, DC
National Organization for Rare Disorders, New Fairfield, CT
National Patient Travel Center, Virginia Beach, VA
National Society of Genetic Counselors, Wallingford, PA
National Spasmodic Torticollis Association, Fountain Valley, CA
National Tay-Sachs & Allied Diseases Association, Boston, MA
National Urea Cycle Disorders Foundation, La Canada, CA
Noonan Syndrome Support Group, Upperco, MD
Organic Acidemia Association, Plymouth, MN
Orphan Medical, Minnetonka, MN
Osteogenesis Imperfecta Child Advocacy (OICA), Woodville, WI
Osteogenesis Imperfecta Foundation, Gaithersburg, MD
Osteogenesis Imperfecta Parents' Support Group, San Diego, CA
Parents of Galactosemic Children, Sparks, NV
Pediatric/Adolescent Gastroesophageal Reflux Association (PAGER), Germantown, MD
Pediatric Neurotransmitter Disease (PND) Association, Plainview, NY
Periodic Paralysis Association, Monrovia, CA
Peutz-Jeghers Syndrome Online Support Group
Pierre Robin Network, Fowler, IL
Polyarteritis Nodosa Support Group (PNSG), Pittsburgh, PA
Polychondritis Educational Society, Somerton, AZ
PRISMS (Parents and Researchers Interested in Smith-Magenis Syndrome), Franconia, NH
Project DOCC – Delivery of Chronic Care, Oyster Bay Cove, NY
PXE (Pseudoxanthoma Elasticum) International, Sharon, MA
Reflex Sympathetic Dystrophy Syndrome Association, Milford, CT
Restless Legs Syndrome Foundation, Rochester, MN
Rupertus Foundation to Cure ALS, Virginia

Sarcoid Networking Association, Sumner, WA
Scleroderma Foundation, Byfield, MA
Sickle Cell Disease Association of America, Culver City, CA
Sigma Tau Pharmaceuticals, Gaithersburg, MD
Society for Progressive Supranuclear Palsy, Baltimore, MD
Sotos Syndrome Support Association, Pueblo, CO
Stickler Involved People, Augusta, KS
Sturge-Weber Foundation, Mt. Freedom, NJ
Tourette Syndrome Association, Bayside, NY
Transkaryotic Therapies, Inc., Cambridge, MA
Trigeminal Neuralgia Association, Barnegat Light, NJ
Trimethylaminuria Support Group, New York, NY
Tuberous Sclerosis Alliance, Silver Spring, MD
Tyler for Life Foundation, Winston, GA
Von Hippel-Lindau Family Alliance, Brookline, MA
United Mitochondrial Disease Foundation, Monroeville, PA
Wegener's Granulomatosis Association, Kansas City, MO
Wilson's Disease Association, Brookfield, CT
Zeroderma Pigmentosum Society, Poughkeepsie, NY
XLH (X-linked Hypophosphatemic Rickets) Network, Bowie, MD

Attachment II
Department of Health and Human Services
Office of Inspector General

In a Department of Health and Human Services report entitled “The Orphan Drug Act – Implementation and Impact (May, 2001, OEI-09-00-00380), the Office of Inspector General concluded that:

“The Orphan Drug Act’s incentives and the Office of Orphan Products Development’s clinical superiority criteria motivate drug companies to develop orphan products. Since Congress passed the Orphan Drug Act of 1983, the Food and Drug Administration has awarded more than 1,000 designations and approved more than 200 products.

Advocates report that orphan products are usually accessible to patients. Orphan products are usually accessible, although they can be costly and in limited supply. Insurance typically pays for the treatments, and companies offer patient assistance programs to help patients obtain their products.

The Office of Orphan Products Development provides a valuable service to both companies and patients. Companies report an excellent relationship with this office, which awards orphan product designations and disseminates public information about orphan products.

Orphan products meet the legal prevalence limit, and most fall well below the threshold of 200,000 patients. Average patient population has climbed since 1983 but remains well below the legal limit.”

Attachment III

Grant Supported Products with Marketing Approval

Product: 4-methylpyrazole (trade name Antizole); Fomepizole
Indication: Ethylene Glycol and Methanol Poisoning
Approval Date: 12/04/1997
Institution: Orphan Medical, Inc.
Investigator: Dr. Dayton Reardan

Product: Actimmune
Indication: Osteopetrosis
Approval Date: 02/11/2000
Institution: Medical University of South Carolina
Investigator: Dr. Lester Key

Product: Auditory Brainstem Implant
Indication: Bilateral deafness
Approval Date: 10/24/00
Institution: Cochlear Corp.
Investigator: Dr. Steven J. Staller

Product: Anti-TNF (cA2) (trade name Remicade)
Indication: Severe Crohns Disease
Approval Date: 08/24/1998
Institution: Centocor, Inc.
Investigator: Dr. Richard McCloskey

Product: Baclofen Intrathecal (trade name Lioresal)
Indication: Severe Spasticity
Approval Date: 06/25/1992
Institution: Rush-Presbyterian-St. Lukes' Medical Center
Investigator: Dr. Richard Penn

Product: Betaine (trade name Cystadane)
Indication: Homocystinuria
Approval Date: 10/20/1996
Institution: University of Virginia
Investigator: Dr. William Wilson

Product: Busulfan IV
Indication: Bone Marrow Ablation
Approval Date: 02/04/1999
Institution: UT MD Anderson Cancer Center
Investigator: Dr. Borge Andersson

Product: Cladribine (trade name Leustatin)
Indication: Mycosis fungoides and hairy cell leukemia
Approval Date: 03/01/1993
Institution: Scripps Research Institute
Investigator: Dr. Ernest Beutler

Product: Clonidine (trade name Duraclon)
Indication: Intractable pain in cancer patients
Approval Date: 10/02/1996
Institution: Wake Forest University
Investigator: Dr. James Eisenach

Product: CroFab
Indication: Crotalid snake bites
Approval Date: 10/02/00
Institution: Therapeutic Antibodies, Inc.
Investigator: Dr. Richard C. Dart

Product: Cysteamine (trade name Cystagon)
Indication: Nephropathic Cystinosis
Approval Date: 08/15/1994
Institution: University of California, San Diego
Investigator: Dr. Jerry Schneider

Product: Ganciclovir Intravitreal (trade name Vitrasert)
Indication: CMV Retinitis
Approval Date: 03/04/1996
Institution: University of Kentucky Research Foundation
Investigator: Dr. Thomas Smith

Product: Glatiramer acetate (trade name Copaxone)
Indication: Relapsing remitting multiple sclerosis
Approval Date: 12/20/1996
Institution: Lemmon Company
Investigator: Dr. Yafith Stark

Product: Histrelin Acetate (trade name Supprelin)
Indication: Central precocious puberty
Approval Date: 12/24/1991
Institution: Massachusetts General Hospital
Investigator: Dr. Paul Boepple

Product: In-Exsufflator (trade name Cofflator)
Indication: Assist Ventilator dependent patients
Approval Date: 02/01/1993
Institution: University of Medicine and Dentistry of New Jersey
Investigator: Dr. John Bach

Product: Iobenguane sulfate I-131
Indication: Localization of Pheochromocytoma
Approval Date: 03/24/1994
Institution: University of Michigan
Investigator: Dr. Brahm Shapiro

Product: Levocarnitine (trade name Carnitor)
Indication: Primary and Secondary Carnitine Deficiency of Genetic Origin
Approval Date: 12/16/1992
Institution: Duke University
Investigator: Dr. Charles Roe

Product: Nafarelin Acetate Intranasal (trade name Synarel)
Indication: Central Precocious Puberty
Approval Date: 02/06/1992
Institution: Baylor College of Medicine
Investigator: Dr. John Kirkland

Product: Neurostimulator implantable electrodes
Indication: Quadra-paraplegia with loss of hand function
Approval Date: 08/18/1997
Institution: Case Western Reserve University
Investigator: Dr. Paul Peckham

Product: Pegademase (trade name Adagen)
Indication: ADA replacement in Severe Combined Immunogenicity Disease
Approval Date: 03/21/1990
Institution: Enzon, Inc.
Investigator: Dr. Abraham Abuchowski

Product: Pulmonary angioscope
Indication: Visualization of pulmonary emboli
Approval Date: 01/31/1989
Institution: Regents of the University of California
Investigator: Dr. Deborah Shure

Product: Sodium phenylbutyrate
Indication: Urea cycle disorders
Approval Date: 04/30/1996
Institution: Johns Hopkins University
Investigator: Dr. Saul Brusilow

Product: Succimer (trade name Chemet)
Indication: Lead Poisoning in Children
Approval Date: 01/30/1991
Institution: The Kennedy Institute
Investigator: Dr. J. Julian Chisolm

Product: Sucrase enzyme
Indication: Sucrase-isomaltase deficiency
Approval Date: 04/09/1998
Institution: Hartford Hospital
Investigator: Dr. Jeffrey Hyams

Product: Tobramycin for inhalation (trade name Tobi)
Indication: Management of CF patients with Pseudomonas Aeruginosa
Approval Date: 12/22/1997
Institution: Pathogenesis Corporation
Investigator: Dr. Alan Montgomery

Product: Tretinoin (trade name Vesanoid)
Indication: Acute Promyelocytic Leukemia
Approval Date: 11/22/1995
Institution: Memorial Hospital for Cancer and Allied Diseases
Investigator: Dr. Raymond Warrell, Jr.

Product: Zinc Acetate (trade name Galzin)
Indication: Wilson's Disease
Approval Date: 01/28/1997
Institution: University of Michigan
Investigator: Dr. George Brewer

Attachment IV



FDA Office of Orphan Products Development FY2001 Accomplishments

FDA's Office of Orphan Products Development (OPD) encourages the development of drugs, biologics, medical devices, and medical foods for rare diseases and conditions by offering the sponsors of these products financial incentives.

Since the Orphan Drug Act was enacted in 1983, FDA's Office of Orphan Products Development (OPD) has designated 1,152 products to treat many rare conditions. Of these, 228 orphan products are now available to treat a potential patient population of more than 11 million people in the U.S.

During fiscal year 2001, OPD received 129 applications for orphan designation. The OPD medical and pharmaceutical review staff approved 78 of those applications for orphan status and six orphan products received FDA market approval.

A significant component of OPD is the Orphan Products Grants Program, which funds studies to develop treatments or diagnostic products for rare diseases. Since the Orphan Drug Act began, FDA has funded 150 million dollars in rare disease research.

In 2001, Congress appropriated 12.5 million dollars for the program, which provided funds for both new studies, and for the continuation of previously funded studies.

The grants program funded 24 new studies to test products to treat rare diseases in 2001 and currently, 84 OPD grant studies are underway.

OPD staff made ten grant site visits to advise and support clinical investigators. Since 1983 the orphan products grant program has led to the development and approval of 29 new products to treat or diagnose rare diseases.

OPD continues to facilitate the development of treatments for rare diseases worldwide. This year the OPD director consulted with interested European Community legislators, and spent considerable time briefing and mentoring members of the Committee on Orphan and Medicinal Products of the European Agency for the Evaluation of Medicinal Products. The OPD hosted visits from foreign legislative organizations currently investigating new strategies for orphan product development.