TESTIMONY SUBMITTED FOR RECORD

To The

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

By The

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Regarding

FY 2004 APPROPRIATIONS FOR THE ORPHAN PRODUCTS RESEARCH GRANT PROGRAM AT THE FOOD AND DRUG ADMINISTRATION (FDA)

National Organization for Rare Disorders (NORD)
Testimony Submitted for the Record Regarding
FY 2004 Funding for the Food and Drug Administration's
Orphan Product Research Grant Program
April 2003

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 Grants Program administered by the Office of Orphan Product Development (OOPD) at the Food and Drug Administration (FDA).

On November 6, 2002, President George W. Bush signed the *Rare Diseases Orphan Product Development Act*, P.L. 107-281, sponsored by Representative Mark Foley. The purpose of the Act is to "**increase the national investment in the development of diagnostics and treatments for patients with rare diseases and disorders**," as follows:

> *Sec. 3. FOOD AND DRUG ADMINISTRATION; GRANTS AND CONTRACTS FOR THE DEVELOPMENT OF ORPHAN DRUGS.*
>
> *Subsection (c) of section 5 of the Orphan Drug Act (21 U.S.C. 360ee(c)) is amended to read as follows:*
>
> *"(c)" For grants and contracts under subsection (a), there is authorized to be appropriated such sums as already have been appropriated for fiscal year 2002,and $25,000,000 for each of the fiscal years 2003 through 2006."*

As NORD, and the 25 million Americans affected by rare diseases celebrate the 20th anniversary of the passage of the *Orphan Drug Act,* we respectfully request that this Committee reconfirm its commitment to the rare disease community through increased funding for research on needed diagnostics and therapeutics. Specifically, we request that this Committee support an increase in funding for the FDA's Orphan Product Research Grants program to the $25 million authorized in the Rare Diseases Orphan Product Development Act (P.L. 107-281), and for each of the fiscal years 2005 through 2008.

<u>Background</u>

In 1982, the U.S. Congress passed the *Orphan Drug Act, (ODA)*, P.L. 97-414, and on January 4,1983, President Ronald Reagan signed it into law. Both the Congress and the Administration recognized that "a pharmaceutical company which develops an orphan drug may reasonably expect the drug to generate relatively small sales in comparison to the cost of developing the drug and consequently to incur a financial loss." It also found that, "there is reason to believe that some promising orphan drugs will not be developed unless changes are made in the applicable Federal laws to reduce the costs of developing such drugs and to provide financial incentives to develop such drugs."[i]

Financial incentives of the ODA include:

- Seven years marketing exclusivity for the first company to develop an orphan drug for a rare disease;
- User fee waiver;
- Tax credits for the costs of clinical research;
- Establishment the FDA Orphan Product Research Grants program to support small clinical trials on new orphan drugs, biologics, devices and medical foods;
- The law defines a rare disease or condition as any disease or condition which "(A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug."[ii]

Orphan Products Defined

- "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. For example, only 10 products specifically for the treatment of rare diseases were developed by the pharmaceutical industry during the 10 years prior to 1983;
- Since 1983, the FDA has approved 238 orphan drugs for marketing, and more than 900 additional orphan drugs are in the research pipeline
    - 85% are used for serious and/or life-threatening diseases
    - 31% are for rare cancers
    - 11% are for metabolic disorders
    - 50% are for pediatric uses
    - 20% of orphan designations are for novel biotechnology products;
- According to the FDA Office of Orphan Product Development, these currently marketed orphan drugs are helping over 11 million Americans and millions more around the world.[iii]

Orphan Products Research Grants Program

- This Subcommittee created the FDA Orphan Products Research Grants program in FY 1982 to provide funding for pivotal clinical trials on new orphan drugs, medical devices, and medical foods for rare diseases;
- Of the 238 orphan products currently approved for marketing, 29 (25 drugs and 4 medical devices) have been developed with funding from the FDA's orphan product research grants. These small research grants are critically important to academic scientists trying to develop preliminary data they can use to attract commercial sponsors who will develop their treatment and bring it to the American market. They are also important to small companies developing sufficient data to attract investment capital;[iv]

- Twenty-one of the 29 products developed through funding from the FDA's Orphan Products Research Grants Program were awarded to investigators at academic centers. The remainder went to start-up firms (see attached), thus "bridging the gap between basic research, clinical development and marketing approval;"[v]
- Approximately 80 applications for new orphan product research grants are received each year, but until now only 20 percent of those new applications have actually been funded annually;
- 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, This unique research grant program is the quintessential model for a successful government/industry partnership, filling a major gap between academic research and the private sector, and creating lifesaving products 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 Grants Program that allows the children's lungs to expand and breathe;
    - Narcolepsy, Cystic fibrosis, Crohn's disease, and multiple sclerosis drugs are on the market today only because these grants supported some of their clinical research.

Conclusion

Many diseases and conditions 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. The FDA's Orphan Products Research Grants program enables scientists to develop the preliminary data necessary to show that a drug, biologic, device or food is safe and probably effective, making commercial development less risky. Only then will a company be interested in adopting the product and bringing it through the FDA approval process.

The National Institutes of Health (NIH) has catalogued 6,000 rare diseases, some of which are familiar ailments including Tourette Syndrome, Sickle Cell Anemia and Hemophilia. Yet there are thousands of others devastating rare diseases that are unfamiliar to the public and the medical community.

- Fibrodysplasia ossificans progressive (FOP) is a genetic disorder "in which the body transforms its muscles, tendons, and ligaments into bone." Patient population: 125.

- Sturge-Weber Syndrome is a condition characterized by excessive blood vessel growth, accumulation of calcium in the brain and seizures. Patient population: less than ten thousand.
- Angelman Disease is characterized by severe mental retardation, prolonged inappropriate laughter, facial abnormalities, and impaired movement control. Patient population: approximately 700. [vii]

For the patients affected by these and thousands of other rare diseases, the prospects for a cure or the discovery of a therapy to alleviate symptoms have been dim. Diagnosis takes from one to six years in 35 percent of the cases, and more than seven years in 15 percent.[viii] Even when the cause of the disease is discovered, (e.g., a genetic defect, infectious agent, etc.), most pharmaceutical companies would be very hesitant to invest in development of a new treatment unless there is evidence from small clinical trials indicating that an experimental treatment will work. These small research grants from the FDA provide support for academic researchers and small companies so they can develop the evidence necessary to attract commercial sponsors.

The FDA's Orphan Products Research Grants Program is not new. It has a 21-year record of accomplishment, and it has already been responsible for the development of 29 life-saving orphan products that would not be on the market today if this program had not existed. When Congress passed the *Rare Diseases Orphan Product Development Act* last year, it sent a strong signal to rare disease patients in every state of the union that it recognizes the critical importance of these research grants, it salutes the progress that the ODA has pioneered in the last two decades, and Congress implicitly intends to appropriate $25 million to the FDA's Orphan Product Research Grants Program which represents only $1 for every rare disease patient in the United states.

NORD, on behalf of the 25 million medically disenfranchised Americans and their families affected by rare "orphan" diseases, respectfully requests that the members of this Subcommittee appropriate no less than $25 million to the FDA Orphan Products Research Grants Program for FY 2004 and for each of the fiscal years 2005 through 2008.as provided for in the *Rare Diseases Orphan Product Development Act*. This funding will fill the void between government and the private sector, and propel new treatments forward from academic laboratories to patients' bedsides and ultimately to our local pharmacies. Your compassion and insight will put new orphan drugs and devices into the waiting hands of critically ill patients.

About NORD

NORD is a federation of approximately 130 voluntary health organizations and over 50,000 individual patients, healthcare providers and clinical researchers dedicated to helping the 25 million people in the United States affected by rare "orphan" diseases. NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research and service.For additional information, please contact Diane E. Dorman, Vice President for Public Policy, in NORD's Washington Office at (202) 258-6457 or ddorman@rarediseases.org.

Thank you.

Attachment I

[DOCID: f:publ281.107]

[[Page 116 STAT. 1992]]

Public Law 107-281
107th Congress

An Act

To amend the Federal Food, Drug, and Cosmetic Act with respect to the development of products for rare diseases. NOTE: Nov. 6, 2002 - [H.R. 4014]

Be it enacted by the Senate and House of Representatives of the United States of America in Congress NOTE: Rare Diseases Orphan Product Development Act of 2002 assembled,

SECTION 1. NOTE: 21 USC 301 note. SHORT TITLE.

This Act may be cited as the ``Rare Diseases Orphan Product Development Act of 2002".

SEC. 2. NOTE: 21 USC 360ee note. FINDINGS AND PURPOSES.

(a) Findings.--Congress makes the following findings:

(1) Rare diseases and disorders are those which affect small patient populations, typically populations smaller than 200,000 individuals in the United States. Such diseases and conditions include Huntington's disease, amyotrophic lateral sclerosis (Lou Gehrig's disease), Tourette syndrome, Crohn's disease, cystic fibrosis, cystinosis, and Duchenne muscular dystrophy.

(2) For many years, the 25,000,000 Americans suffering from the over 6,000 rare diseases and disorders were denied access to effective medicines because prescription drug manufacturers could rarely make a profit from marketing drugs for such small groups of patients. The prescription drug industry did not adequately fund research into such treatments. Despite the urgent health need for these medicines, they came to be known as ``orphan drugs" because no companies would commercialize them.

(3) During the 1970s, an organization called the National Organization for Rare Disorders (NORD) was founded to provide services and to lobby on behalf of patients with rare diseases and disorders. NORD was instrumental in pressing Congress for legislation to encourage the development of orphan drugs.

(4) The Orphan Drug Act created financial incentives for the research and production of such orphan drugs. New Federal programs at the National Institutes of Health and the Food and Drug Administration encouraged clinical research and commercial product development for products that target rare diseases. An Orphan Products Board was established to promote the development of drugs and devices for rare diseases or disorders.

(5) Before 1983, some 38 orphan drugs had been developed. Since the enactment of the Orphan Drug Act, more than 220 new orphan drugs have been approved and marketed in the [Page 116 STAT. 1993]] United States and more than 800 additional drugs are in the research pipeline.

(6) Despite the tremendous success of the Orphan Drug Act, rare diseases and disorders deserve greater emphasis in the national biomedical research enterprise.

(7) The Food and Drug Administration supports small clinical trials through Orphan Products Research Grants. Such grants embody successful partnerships of government and industry, and have led to the development of at least 23 drugs and four medical devices for rare diseases and disorders. Yet the appropriations in fiscal year 2001 for such grants were less than in fiscal year 1995.

(b) Purposes.--The purpose of this Act is to increase the national investment in the development of diagnostics and treatments for patients with rare diseases and disorders.

SEC. 3. FOOD AND DRUG ADMINISTRATION; GRANTS AND CONTRACTS FOR THE DEVELOPMENT OF ORPHAN DRUGS.

Subsection (c) of section 5 of the Orphan Drug Act (21 U.S.C. 360ee(c)) is amended to read as follows:

``(c) NOTE: Appropriation authorization. For grants and contracts under subsection (a), there are authorized to be appropriated such sums as already have been appropriated for fiscal year 2002, and $25,000,000 for each of the fiscal years 2003 through 2006."

SEC. 4. TECHNICAL AMENDMENT.

Section 527(a) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360cc(a)) is amended in the matter following paragraph (2)--

(1) by striking ``, of such certification,"; and (2) by striking ``, the issuance of the certification,".

Approved November 6, 2002.

LEGISLATIVE HISTORY--H.R. 4014:

HOUSE REPORTS: No. 107-702 (Comm. on Energy and Commerce).
CONGRESSIONAL RECORD, Vol. 148 (2002):

Oct. 1, considered and passed House.
Oct. 17, considered and passed Senate.

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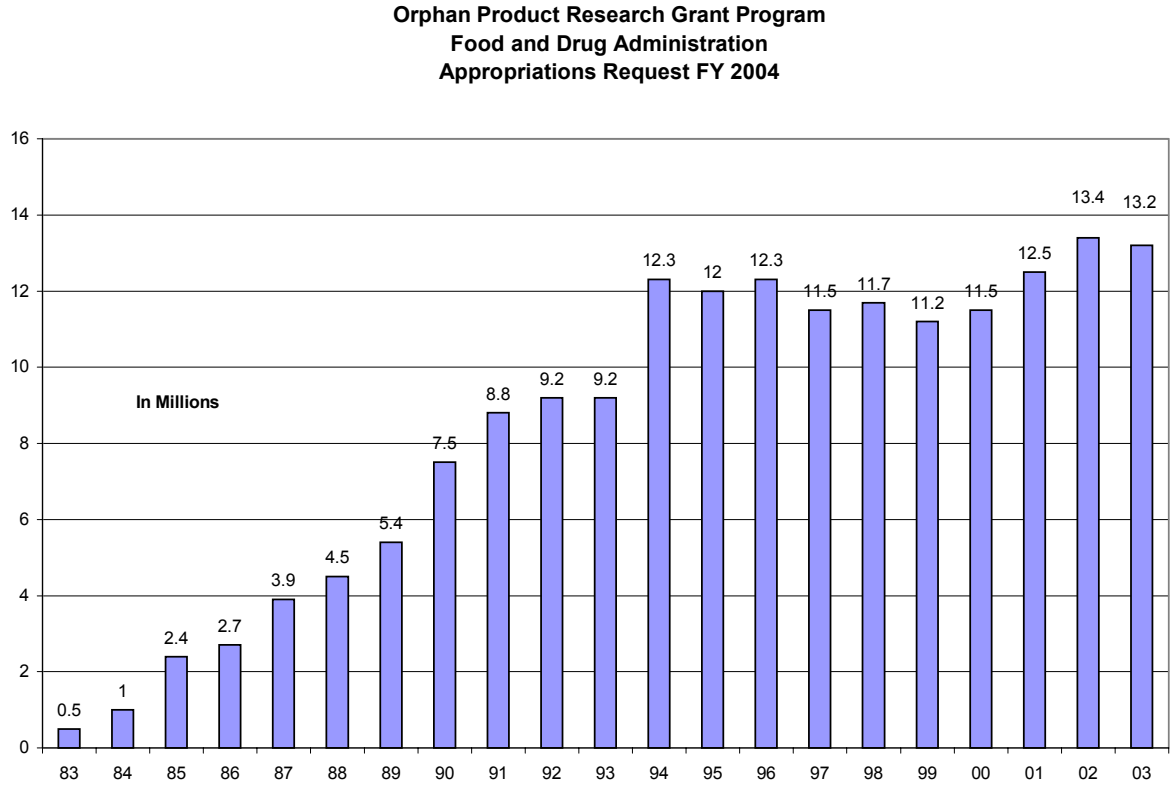
Attachment II



Attachment III

U.S. Food and Drug Administration

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 NJ
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: Nitisinone (trade name Orfadin)
Indication: Treatment of tyrosinemia type 1.
Approval Date: 01/18/2002
Institution: Swedish Orphan AB
Investigator: Dr. Ronald Leonardi

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

Product: Gamma-hydroxybutyrate
Indication: Narcolepsy
Approval Date: 07/17/02
Institution: University of Arkansas for Medical Sciences
Investigator: Lawrence Scrima, Ph.D.

Updated February 20, 2003

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[i] The *Orphan Drug Act*, Public Law 97-414.
[ii] The *Orphan Drug Act*, as amended October 1984, P.L. 98-551
[iii] Haffner, Marlene E., Whitley, Janet and Moses, Marie. Two decades of orphan product development, *Nature Reviews*, October 2002, pp. 821-825.
[iv] "The Orphan Drug Act has proven particularly helpful to the biotechnology industry that emerged in the years following passage. This young, volatile industry is heavily dependent on private capital to fund research and development." *The Orphan Drug Act, Implementation and Impact.* DHHS, Office of Inspector General, OEI-09-00-00380, May 2001.
[v] Haffner, et al.
[vi] Maeder, Thomas. Adopting Orphan Diseases. *Red Herring*, January 16, 2001, pp. 128.134.
[vii] Maeder, p. 130.
[viii] Report of the National Commission on Orphan Diseases, Publication Number HRP-090-7248, United States Government Printing Office, February, 1989.