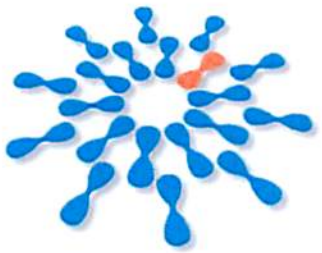

NORD
National Organization for Rare Disorders

Testimony of

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Before the

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"Treating Rare and Neglected Pediatric Diseases: Promoting the Development of New Treatments and Cures"

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I wish to thank Chairman Harkin, Senator Enzi and other distinguished members of this Committee for inviting me to testify today regarding a topic that is extremely important to my organization—the development of safe, effective treatments and cures for the millions of American children afflicted with rare diseases.

My name is Diane Dorman, and I am the Vice President for Public Policy of the National Organization for Rare Disorders (NORD). NORD is a non-profit organization with offices in Washington DC and Danbury, Connecticut, that provides a voice to the nearly 30 million Americans with rare diseases. It was established in 1983 by patient organization leaders who served as the primary consumer advocates responsible for enactment of the *Orphan Drug Act.*

In the United States, there are between 6,000 and 7,000 diseases considered rare, according to the National Institutes of Health. To be classified as "rare", a disease must be believed to affect fewer than 200,000 Americans. This is the definition used by the Food and Drug Administration and by the National Institutes of Health.

Although each individual rare disease affects no more than 200,000 people, and some affect only a few hundred or even a few dozen, rare diseases in the aggregate affect approximately one in 10 Americans. There are certain issues and challenges that are common to all people with rare diseases, no matter where they fall on this spectrum.

Since many of these diseases are genetic, many of the patients are children. It is believed that more than two-thirds of the individuals affected by rare diseases in the U.S. are children.

Furthermore, most rare diseases are serious and chronic or lifelong. Many are life-threatening. A recent editorial in the journal, *Nature,* noted that among patients afflicted with any of the 350 most common rare diseases, 27% will not live to see their first birthday.

My colleagues and I have a great deal of one-on-one contact with rare disease patients and their families, as well as with patient organization leaders. As you might imagine, some of the most difficult phone conversations we have are with parents of young children who have rare diseases. These families are faced with very difficult issues such as diagnosis delay, too little research, too few treatments, reimbursement or other financial issues, and a general sense of having been abandoned by our nation's health care system.

We very much appreciate the invitation to speak to you today. Since the topic is broad, I would like to organize my comments into the following sub-topics to reflect what we see as the primary issues and challenges through our daily contact with the families of children affected by rare diseases.

Pre-clinical Challenges

Families often contact NORD just after having received a diagnosis for a child. They are typically still in a very fragile state in which they are desperately seeking information about the disease and hoping to find resources, medical experts, and opportunities to participate in clinical trials.

You can imagine how difficult it is to have to tell families, as we frequently do, that not only is there no treatment for their child's disease but there is no research in progress. The sad reality for far too many people with rare diseases is that no one...at NIH, at a teaching hospital, on a university campus, or in industry...is doing research on their disease at this time. And no research means no hope for the future.

Part of the problem is a lack of natural history data, validated animal models, patient registries and prevalence/incidence data on rare diseases. These basic tools form the foundation for clinical research, and they are a necessary first step.

The rare disease patient community is highly motivated and resourceful. Many of the few patient registries and other research resources that exist at this time have been funded or launched by patient organizations. But patients can't do it alone. There must be federal funding and federal guidelines and encouragement for the establishment of these basic tools for research. With such support, I can guarantee that patients and patient organizations will be active partners in moving studies forward.

Clinical Challenges

Because of the small patient populations, and the fact that rare disease patients are scattered around the globe, clinical research aimed at developing treatments for the rare disease community is by its very nature more expensive and more challenging than other research. The requirements for clinical trials need to be stringent enough to provide reasonable assurance of safety and efficacy for patients, but they must also take into account the fact that these diseases present a unique set of challenges for researchers. In addition, patients with rare diseases are generally willing to accept higher levels of risk than other patients may be motivated to do.

At this time, a significant portion of rare-disease research is funded by the patient community. While NIH and particularly the NIH Office of Rare Diseases Research have made admirable strides in recent years in focusing greater attention on the need for research on these diseases, for many of the very rare diseases it is still too often the patient community that funds and drives research through golf tournaments, raffles, even bake sales and car washes. As a society, it is wrong for us to expect people with devastating diseases to fund the search for their treatments. We need to make a more significant effort at the federal level to fund studies of rare diseases and incentivize researchers to pursue them.

Regulatory Challenges

NORD hosted a Summit in May 2009 at which we drew together approximately 300 participants from NIH, FDA, patient organizations and industry to focus on how to accelerate the development of treatments for rare diseases and how to ensure patient access to treatments. A point made by several speakers was that industry frequently develops a second product for a disease that already has one or more treatments rather than addressing a disease that has no treatment at all. This was attributed, at least in part, to reduced regulatory uncertainty once the first product is brought to market.

A few weeks ago, the chairman of NORD's board of directors addressed a public hearing hosted by the FDA. His recommendation, on behalf of NORD, was for FDA to reduce regulatory uncertainty and increase consistency by implementing a statement of policy on regulation of therapies for rare diseases.

Only about 200 of the nearly 7,000 rare diseases currently have FDA-approved treatments. To NORD and the patient community, it appears as if the low-hanging fruit have been harvested since enactment of the *Orphan Drug Act* in 1983, but much more remains to be done.

While orphan drugs are reviewed with the same standards of safety and effectiveness as other drugs, FDA publicly acknowledges that it exercises its scientific judgment in taking into account the special challenges of developing treatments for very small patient populations. However, without a statement of policy on rare diseases and orphan products, it is not possible to ensure consistency in that process.

Other uncertainties in the regulatory arena include the need for identification and agreement on clinical endpoints and surrogate markers, the need for greater transparency and understanding of the regulatory process, and the need to have regulators who understand the special challenges of developing orphan products. NORD applauds the recent creation of an Associate Director for Rare Diseases position in FDA's Center for Drug Evaluation and Research (CDER) and the inclusion in the current Senate Appropriations bill of funding for staff to assist the Associate Director.

Reimbursement Challenges

Certain metabolic diseases, such as phenylketonuria, require specialized infant formulas and medical foods as a very important part of treatment. Patients who don't get these special foods may suffer very serious consequences, including severe mental retardation. However, insurers (including Medicaid) don't always reimburse for the cost of these foods since they are not prescription drugs.

Only about a third of the states currently mandate reimbursement for the costs of specialized infant formulas and medical foods. Since these foods have been demonstrated to be an important part of medical treatment for children with certain diseases, NORD feels strongly that access should not be hindered as a result of inability to pay. We would like to see a federal mandate to ensure that no child is denied a needed medical food because of failure by insurers to provide coverage.

Another reimbursement issue is the off-label use of drugs for rare diseases. It has been estimated that 90% of the nearly 30 million Americans with rare diseases are treated off-label simply because there is no FDA-approved therapy for them. As the cost of healthcare continues to skyrocket, insurers (both public and private) increasingly are denying coverage for off-label use of drugs, biologics, and medical devices on the basis that such therapy is experimental. For people with rare diseases who have no other options, this is becoming a serious problem.

NORD does not want to discourage pharmaceutical and biotechnology companies from conducting clinical trials to obtain FDA approval for these additional uses. However, we feel that legislation might be employed appropriately to help rare-disease patients and families obtain reimbursement for off-label treatment that is medically necessary when no FDA-approved options are available to them.

Humanitarian Use Devices

While we've been speaking primarily of orphan drugs and medical foods, clearly there is a need for the development of pediatric medical devices for many children with rare diseases. And NORD feels strongly that it is important to emphasize that children are not just small adults. Sick children need medical devices and drugs developed specifically for their unique needs, taking into account their smaller size, growing bodies, and active lifestyles.

To illustrate the challenges inherent in development of medical devices for this particular population, we cite the experience of Dr. Robert Campbell, a pediatric orthopedic surgeon on NORD's Medical Advisory Committee, who is affiliated with the Children's Hospital of Philadelphia.

Dr. Campbell invented, developed and brought to market a pediatric device known as the expandable titanium rib that has saved the lives of hundreds of infants and children who have a condition known as thoracic insufficiency syndrome. Prior to his work, there was no treatment for children with this condition, and most ultimately died because there was not enough room for their lungs to expand as the children grew. (Please see attachment 1)

Dr. Campbell's research was made possible by a small seed-money grant from NORD, when no other funding was available. Later, he was able to obtain funding to continue the research through the FDA Orphan Product Development grant program. Ultimately, the device he developed—the titanium rib—was approved by FDA as a Humanitarian Use Device. Because no company was interested in manufacturing it, Dr. Campbell also took it upon himself to find a small company that would—essentially for humanitarian reasons—agree to manufacture and market the titanium rib.

The families helped by this medical device remain tremendously grateful to Dr. Campbell and his colleagues. But there are many others with other rare diseases who may not have a Dr. Campbell, and they need help, too.

A complicating factor is that, while FDA considers HUDs to be approved, they must still be reviewed by IRBs. As a consequence, insurers (both public and private) consider them experimental and may not reimburse for them. In addition, while pediatric HUD developers can now realize a profit, this is not the case for all humanitarian devices. The prohibition against developers profiting from these devices needs to be lifted.

Medical Education

NORD works very closely with the medical community, and we know that our nation is blessed with a caring and dedicated medical establishment. However, we feel that medical education in the United States does not adequately address issues and challenges related to rare diseases, and is not at this time encouraging enough young scientists to engage in both research and clinical care related to rare diseases. Given the fact that approximately one in 10 Americans are affected by rare diseases, we believe a greater emphasis on these diseases is warranted in our centers of medical education.

One of the primary problems encountered by rare-disease patients and families is delay in obtaining an accurate diagnosis. In 2003, NORD partnered with Sarah Lawrence College on a study to replicate, on a smaller scale, an earlier study by the federal government of problems experienced by people with rare diseases. Sadly, our study showed that the diagnosis problem remained essentially unchanged since the federal government's study done in 1989.

Some Current Initiatives that Bring Hope to Patients

Currently, NORD is working with FDA, NIH and others to address some of the problems outlined above and to accelerate the development of rare disease therapies. These initiatives include:

- A three-day training course for investigators from academia and small biotechnology and pharmaceutical companies involved in conducting research to develop treatments for rare diseases. This course will be taught by experienced faculty from academia, industry, NIH and FDA, and is being sponsored by NORD, FDA, NIH and Duke University. It will result in the development of a handbook for rare-disease investigators.
- A task force instituted by NORD, in which NIH and FDA have agreed to work together to examine the interface between the two agencies, identify weaknesses, and find ways to work together more effectively to facilitate the development of safe, effective treatments for patients. This task force has already had several meetings.
- A series of orphan designation workshops being hosted by the FDA Office of Orphan Products Development, in partnership with NORD and others, to de-mystify the process of getting orphan designation for a product in development as a rare-disease treatment.
- A series of focus groups, hosted and sponsored by NORD, to gather information from academic researchers, patient advocates, the investment community, and the biopharmaceutical industry to help NIH and FDA review current practices and consider possible improvements.
- An increasingly global response to the needs of rare disease patients, as evidenced by the partnership of NORD and its European counterpart, the European Rare Disease Patient Organization or EURORDIS.
- The launch of a Congressional Rare and Neglected Diseases Caucus, advocated by NORD and its partners, to help focus attention on these important issues and how to address them.

Our Recommendations

In general, our recommendations to this Committee, reflecting what we've learned over the past 27 years as well as our current assessment of the most critical needs of patients at this time, are as follows:

- Continued progress in areas such as the NORD Task Force through which NIH and FDA are identifying ways to work together more effectively; the Rare and Neglected Diseases Congressional Caucus; and the development of a handbook to serve as a roadmap for rare-disease clinical investigators.
- Federal funding and guidelines to develop natural history data, patient registries, epidemiological data and other basic tools to support research.
- Recognition that clinical trials related to rare diseases are, by their nature, different from studies of more common diseases and that they represent a unique set of circumstances and needs.
- A renewed federal commitment to funding research on rare diseases through offices such as the NIH Office of Rare Diseases Research.
- Reduced regulatory uncertainty through steps such as greater transparency of FDA practices and creation of an FDA statement of policy on rare diseases and orphan products.
- Incentives to encourage young investigators to study rare diseases.
- Increased emphasis on rare diseases in our centers of medical education.
- Adoption of the funding proposed in the current Senate Appropriations Bill for the FDA Orphan Products Research Grants Program and to staff the new Associate Director function in FDA CDER.
- Assessment of reimbursement issues related to medical foods and off-label treatment for children with rare diseases.
- Training in rare diseases and orphan product development for FDA reviewers and staff involved in review of orphan products.

In closing, I would like to reiterate several very important points:

1) Among patients afflicted with any of the 350 most common rare diseases, 27% will not live to see their first birthday.
2) Patients and their families are willing to take on a far greater degree of risk than those affected by more common conditions.
3) Understanding the pathogenesis of rare diseases will advance the scientific and medical understanding of common conditions.

Chairman Harkin and Ranking Member Enzi, thank you once again for allowing NORD to testify before you today.

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