



**Statement of Diane Dorman  
Vice President for Public Policy  
National Organization for Rare Disorders (NORD)**

**Before the  
FDA Infectious Diseases Planning Committee  
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Good morning. I want to thank Dr. Timothy Coté for giving me this opportunity share with you the substance and intent of the *Orphan Drug Act* and what it might mean for the development of therapies for infectious diseases in the 21<sup>st</sup> century. I am Diane Dorman, Vice President for Public Policy for the National Organization for Rare Disorders (NORD).

NORD is the consumer organization that advocated for enactment of the *Orphan Drug Act* of 1983. We continue to monitor implementation of the law, especially encouraging research and development of new treatments for rare “orphan” diseases. Our most important mission is to assure that research on rare diseases is widespread and productive, leading to medicines, biologics, devices and diagnostics that will help patients with rare diseases. We support the incentives in law that stimulates companies to do orphan drug research. We want safe and effective products to get to market as quickly as possible.

The *Orphan Drug Act* arose out of a consumer movement. There were many rare disease support groups raising money to fund research on their disease. In cases when a researcher did discover a new treatment, more often than not, no pharmaceutical company was willing to commercialize it. Drug companies generally felt that the cost of research and development for any new treatment outweighed its potential for profit if the market for the drug was small. Even today there are some large pharmaceutical companies that base their R&D decisions on market size and potential profitability.

The orphan drug problem was economic, so it demanded an economic solution. If companies were afraid that they would lose money if they developed an orphan drug, we had to find a way to ensure they would not lose money, and in fact would be able to realize a reasonable profit.

Today, the *Orphan Drug Act* provides for a series of financial incentives to entice drug companies into developing treatments for small populations of patients. The main incentives are:

- Seven years exclusivity during which no other company is allowed to sell the same drug for the same disease.
- FDA orphan product research grants to support pivotal clinical trials.
- A 50 percent tax credit on every dollar a company spends on clinical research.
- Written protocol assistance, meaning FDA will help with clinical research study design.
- And a waiver of FDA user fees for qualifying companies.

Originally, the ODA defined an orphan drug as a drug of limited commercial value when the cost of research and development outweighed its potential for profit. The FDA struggled with that definition, and after two years concluded that the “limited commercial value” definition was unworkable. There was no way for a company to prove the drug would never make a profit. “We are not accountants,” FDA leaders told us. We are doctors. Just give us a definition that enables us to make a medical decision.”

As a consequence, the law was amended in 1985 to define orphan drugs according to population size using incidence and prevalence data: A drug for a disease affecting fewer than 200,000 people in the United States could obtain an orphan drug designation.

How did we get to 200,000? Back then, we knew of treatments for narcolepsy and multiple sclerosis that were not being developed by industry, and the population size for those diseases was estimated at 200,000. Today we know that the prevalence of narcolepsy is much lower, and the prevalence of multiple sclerosis is higher, but we were working with those estimates before 1985.

Also in the 1985 amendments, biologics were added to the *Orphan Drug Act*. Drugs and biologics are regulated under two separate laws: The *Food Drug and Cosmetics Act* (FD&C) regulates drugs, but the *Public Health Service Act* regulates biologics. The *Orphan Drug Act* was an amendment to the FD&C Act, so biologics did not qualify for orphan drug incentives. At that time, the biotechnology industry was in its infancy, and we realized that the proteins, hormones, and enzymes these companies could develop could have therapeutic value for many rare disorders.

It is important to note that the 1985 amendments defining orphan diseases based on prevalence did not discard the older financial definition. So today, a drug can be designated as an orphan drug if it is developed for a disease that affects fewer than 200,000 people in the United States or if it is a drug of limited commercial value.

Over the past 25 years there have been several drugs for tropical diseases designated as orphan drugs. Diseases such as malaria, leprosy, etc., are prevalent in many areas of the world, but they are rare in the United States. Many AIDS drugs were developed as orphan drugs until the prevalence of AIDS exceeded 200,000 during the 1990s. Additionally, antibiotics for cystic fibrosis infections are orphan drugs; cystic fibrosis affects 30,000 Americans.

Any individual orphan drug can have numerous designations if it is used on several diseases or sub-sets of prevalent diseases (e.g., the interferons, Gleevec, thalidomide, etc.)

Has the financial definition ever been used? Yes, some treatments for drug abuse have been designated as orphan drugs even though there are more than 200,000 addicts in the United States. The companies showed that the drug would be unprofitable because the target population is usually uninsured, they have limited income, most patients do not want treatment, and of those who seek treatment, the insured are often Medicaid beneficiaries. Additionally, there are other documented financial disincentives for developing drug abuse treatments such as: restricted distribution (e.g., Methadone which does not go through commercial distribution channels), or drugs that have to be shipped directly from a manufacturer due to a very short shelf life, etc.

Do antibiotics need special incentives? One has to ask why they are not being developed, and then design incentives to address perceived disincentives. No one can claim that antibiotics are not profitable. Perhaps they are not as profitable as a large multi-national pharmaceutical company would wish, but small and mid-size companies are likely candidates.

I want to offer an interesting case study: During the 1980s when HIV infection was emerging, most AIDS patients were dying of a rare type of pneumonia called pneumocystis carinii. Desperate for treatment, some researchers discovered that pneumocystis carinii could be treated successfully with inhaled pentamidine. But pentamidine was an old antibiotic that had been developed to treat Rhodesian sleeping sickness, and the manufacturer had stopped making it several years before (mostly because sales to third-world countries were not profitable).

In this case, consumer organizations worked closely with industry and the FDA to ensure that a dependable supply of pentamidine could be developed. The multi-national company that owned pentamidine was willing to give up its rights, and told us we could have the world's remaining supply of the drug, which was stored in an English warehouse. We lined up a generic company that specialized in the manufacture of liquid drugs, who was willing to copy the original drug and supply it to researchers for clinical trials. We asked a person from the generic drug industry, who was flying to England on other business, to go to the English warehouse. He did, but when he found the warehouse he realized it had a leaky roof, and the entire supply of drug was contaminated.

Nevertheless, the generic company was able to copy pentamidine, and the clinical trials moved forward. By the time an NDA was submitted to the FDA, several drug companies were competing to get the first marketing approval for pentamidine so they could block their competitors with orphan drug exclusivity. Somehow the industry realized that HIV infection would be a profitable market.

And that last point is perhaps the most important for you to remember because it has caused the most controversy over the past 25 years. The law was written for drugs of little commercial value, so why are some orphan drugs as profitable as major blockbusters?

In the American economic landscape, there are no price controls. A manufacturer of goods can charge whatever the market will bear, even for lifesaving medicines. The only constraint is competition. If you have a monopoly on a medicine through orphan drug exclusivity, nothing will drive your price down for seven years if there is no comparable drug.

The most expensive orphan drugs are the biologics, and under current law the FDA has no regulatory pathway to approve a generic biologic. Until they do, the orphan disease community must pay any price a manufacturer demands, sometimes several hundred thousand dollars per year. For a patient with a chronic rare disease, it is equivalent to buying a new house every year for the rest of his or her life. It is not easy to hold on to health insurance if your policy has a lifetime cap, and this is the core of the patient community's love-hate relationship with the industry.

I say this to offer some caution that the blessings brought by the *Orphan Drug Act* over the past quarter century also have a serious downside. Any incentives that would spur development of new treatments for infectious diseases should be fair to manufacturers and fair to patients. Under the patent system, companies ordinarily produce copies of blockbuster drugs, sometimes called “me-too” drugs, that are modestly different from the original product and do not violate the innovators patent. Under orphan drug exclusivity if you develop a “similar” drug for the same disease, you cannot get on the market for seven years unless you can prove that your drug is “clinically superior” to the first drug. This is not an easy thing to do, so you have to be concerned that modestly different antibiotics might be blocked from the market if you adopt legislation based on the *Orphan Drug Act* model.

One final note, today the National Institutes of Health recognizes between 6,000 and 7,000 known rare diseases the majority of which have no treatment specific treatment. As a consequence, ninety percent of the nearly 30 million men, women and children with those rare diseases are treated off-label. Those patients whose diseases are treated with a specific therapy would still be waiting, hoping and praying for help if it were not for the hard fought for incentives of the *Orphan Drug Act*.

For 25 years the rare disease community has fought numerous attempts by the few who have tried to use those incentives for financial gain or to navigate around what is seen as an easy and less expensive roadmap to market. We will continue to fight that fight to ensure that the 90% someday have the same opportunity as those few millions who live better lives today because of the *Orphan Drug Act*.

Thank you.