Remarks of Diane E. Dorman
Senior Director for Public Policy
National Organization for Rare Disorders (NORD)

Public Meeting on the Reauthorization of the Prescription Drug User Fee Act
December 7, 2001

I am Diane Dorman, Senior Director for Public Policy for the National Organization for Rare Disorders (NORD), and on behalf of NORD I want to thank the FDA for the opportunity to share our thoughts and suggestions once again about the reauthorization of the Prescription Drug User Fee Act (PDUFA).

By way of background, NORD participated in the FDA's meeting on PDUFA last September and also testified before the House Energy and Commerce Health Subcommittee this past May to express our views on the effectiveness of the Food and Drug Administration Modernization Act. NORD is also an active member of both the Patient and Consumer Coalition and RxHealthValue.

One of NORD's primary goals is to promote the development of new treatments and cures for rare diseases and to make these therapies accessible to patients. Under the *Orphan Drug Act*, a rare disease is defined as a health condition that affects fewer than 200,000 Americans. Keep in mind that there are more than 6,000 of these disorders, cumulatively affecting an estimated 25 million Americans. NORD's mission, therefore, is enormous and very much reliant on the successes achieved by academic scientists, pharmaceutical and biotechnology companies, medical device manufacturers, and most of all, the Food & Drug Administration (FDA), which regulates these entities.

In the ten years prior to 1983, only 10 products were developed for rare diseases. And that is why Congress established the Office of Orphan Products Development, and provided money for the orphan product research grant program to fund pivotal clinical trials on new orphan drugs, medical devices, and medical foods for rare conditions. These treatments have small potential markets and would not otherwise be attractive to the commercial sector. Today, FDA has approved 220 designated orphan products – proof positive that cooperation between academic researchers, the private sector, the patient community and the federal government can create breakthrough treatments for life-threatening and crippling diseases.

I bring this to your attention only to demonstrate that the FDA, with the support of **all** stakeholders, not just industry support, can and must continue to first and foremost "do no harm." There is the perception that the agency is beholden primarily to the drug industry and continues to play roulette with the lives of patients nationwide. All one has to do is read the headlines -- "*How a New Policy Led to Seven Deadly Drugs*" (Los Angeles Times, David Willman, April 2001) and "*A Question of Speed and Safety*" (Boston Globe, Naomi Aoki, November 28, 2001) - to understand how much of the public, including patients and doctors, have lost faith in the FDA's ability to protect and enhance the public's health.

OIN-0450 TS 6

This is not to say that we want to revert back to "the good old days" when desperately needed therapies took years to reach patients. To the contrary. We all want to see the agency thrive. We all want to see the agency properly and sufficiently funded so it can speed the approval of safe and effective treatments to the American public. But it is this perception of "sleeping with the enemy" that continues to cloud the agency's reputation. A feasible balance must somehow be achieved between speed of approval and safety. A colleague of mine likes to say, "Sunshine is the best disinfectant," and I couldn't agree with him more. Decisions affecting the health and well being of patients must no longer be made behind closed doors. Transparency in the approval process must be achieved if the FDA is to regain the complete trust of the patient community.

Before outlining NORD's position on PDUFA reauthorization, there are several important issues specific to the rare disease community that I wish to highlight. Written into the user fee regulations is an exception for designated orphan drugs. The language reads "a human drug application for a prescription drug product that has been designated as a drug for a rare disease or condition pursuant to section 526 shall not be subject to a fee under subparagraph (A), unless the human drug application includes an indication for other than a rare disease or condition." [1]

Regulations go on to say that in order to qualify for this exemption, a company or entity must qualify under the fee waiver or reduction for small business. At the moment, "FDA generally considers an entity with less than $10 million in annual gross revenues and no corporate parent or funding source with annual gross revenues of $100 million or more, as less likely to be able to continue to provide products that benefits the public health and to develop innovate technology because of user fees."[2]

First and foremost, we want assurances from FDA officials that this exemption will remain in force. Secondly, because both CBER and CDER have a financial stake in the decision to allow an exemption or not, we believe these decisions would be better made by a more independent entity in consultation with the FDA Office of Orphan Products Development. Without this exemption many small and start-up companies would be unable to bring vitally needed orphan products to market. And thirdly, because no allowances were made for inflation, and because the $10 million and $100 million are based on the 1993 economy, the rare disease community will advocate for an increase in the small business exemption, as it relates to orphan products, with an inflation index included.

In the case of medications for very rare disorders, the PDUFA fees may force a company to consider not developing the product or not continuing to make it available – an untenable situation for the rare disease community. For example, congenital sucrase-isolmaltase deficiency is a disorder impacting approximately 100 identified patients in the United States. Although the manufacturer has revenues in excess of $10 million, the sales of *Sucraid R* are such that the payment of PDUFA fees against profit and loss of this product would be significant, perhaps necessitating the company to consider its discontinuation. Another example is a product named *Elliotts B Solution R*. The agents are delivered in a very unique and seldom utilized way (used as a diluent for intrathecally administered methotrexate and cytarabine), so the total revenues for this product are well under $500 million annually. PDUFA fees paid on *Elliotts B Solution* may make the continued availability of this product commercially unviable.

Although revenues in excess of $10 million may sound substantial, development costs are prohibitive for as yet unprofitable or start-up companies, and most entities must consider the contribution of each product individually in order to determine if it will be a contributor or a drain on the "bottom line." While the PDUFA legislation attempts to make exceptions in order that development and commercialization of medications for rare disorders is attractive, the issues and possible solutions should be given serious consideration as future legislative approaches are explored.

Regarding the questions posed for the panelists:

1. **How can FDA ensure that PDUFA goals are met if there continues to be a funding shortfall?**

It is evident that PDUFA goals will continue to be met now and into the future much to the detriment of other critically important programs established to protect the public health. According to a statement made by an FDA official earlier this year, PDUFA-related program funding has risen about 27%. It is only the non-PDUFA programs that suffer. Funds are being siphoned from essential programs such as post-marketing surveillance, health fraud investigations, inspections of IRBs, enforcement, training, management, staff-retention, advertising enforcement, and adverse event reporting — to the tune of 20% — in order to meet the letter of the law. This erosion has created a $200 million shortfall for these programs over the past 10 years.[3]

As a matter of principle, NORD opposes the concept of user fees with its inflexible performance goals and triggers. However, given the current political and economic climate, it is safe to assume that Congress will not fully fund the FDA, sans user fees. I would like to congratulate Congress, however, for recently taking the important first step to adequately fund the agency. Just as the NIH has enjoyed record funding, the agency should also see a doubling of its budget in order to fulfill its increasingly important public health responsibilities.

Whatever the solution, whether it is increased user fees, requiring user fees at the earliest phase of development, or expanding the use of user fees outside of the new drug approval process, a creative solution to this dilemma must be found. With the mapping of the human genome and the increasingly complex biologic and chemical compounds being developed by industry, the United States will only remain in the forefront of medical discovery if, and only if, the FDA is given the necessary resources to fulfill its mandate.

2. **If the funding shortfall persists, should FDA, in order to best protect and promote the pubic health, set review priorities and, if so, how?**

Drugs for serious and life-threatening diseases require different risk-benefit calculations. They should be reviewed more quickly and considered for marketing as early as possible because those suffering with life-threatening diseases, or those with no satisfactory alternative treatment options (especially those with untreatable rare "orphan" diseases) will, more often then not, accept the risks a new drug might pose in exchange for the benefits it may well provide. The FDA should take all steps necessary to ensure that effective new drugs are made available to

patients with these serious and life-threatening conditions as soon in the development process as is practical. However, in recent years it appears that the agency has rushed too many "me-too" drugs through the priority review process when they should have been given standard reviews. We urge the agency to change the way it categorizes "standard" and "priority" reviews.

We believe the overriding success of the agency must NOT be measured by the speed of its work, but rather the completeness and scientific soundness of its work. In order to protect the health and welfare of the American public, a "one size fits all" approach must not be taken.

FDA reviewers should be given the latitude to review new drug applications at a slower rate if it is deemed scientifically and/or ethically necessary, especially when a drug is not a life-saving therapy. It is obvious to me that some of the drugs removed from the market in recent years might have been approved with more adequate labeling **IF** FDA had taken enough time to recognize adverse effects, and had required appropriate labeling when the drugs were first approved.

3. **Should there be flexibility in setting user fees to cover the increased cost of the program?**

Most definitely. The FDA must be able to adapt to the changing marketplace. Stringent appropriations triggers should not obstruct the Agency's ability to efficiently and effectively pursue the goals of ensuring that safe and efficacious products are brought to the marketplace. As currently written, performance goals and mandatory deadlines do not allow for flexibility.

I thank you for this opportunity to express our view and the entire rare disease community looks forward to working with the FDA in the coming months to ensure that the interests of patients and the regard for the public health is upheld.

---

[1] Interim Guidance Document for waivers of and reductions in user fees. Attachment G. July 16, 1993.
[2] Ibid.
[3] Statement made by Jane Axelrad before the annual educational conference of the Food and Drug Law Institute. *FDA Week*. Vol. 7, No. 16, April 20, 2001, p. 12).