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before the

**United States Senate Committee on Health, Education, Labor, and
Pensions**

“Drug User Fees: Enhancing Patient Access and Drug Safety”

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Introduction

Chairman Kennedy, Senator Enzi, and members of the Committee. Thank you for this opportunity to testify today regarding the reauthorization of the Prescription Drug User Fee Act (PDUFA) and pending legislative proposals to enhance the post-market safety of prescription drugs.

I am Diane Dorman, Vice President for Public Policy of the National Organization for Rare Disorders (NORD). We are a leading national non-profit voluntary health agency dedicated to the identification, treatment and cure of rare diseases. There are more than 6,000 of these disorders, cumulatively affecting an estimated 25 million Americans. NORD has a long successful history working with Congress on the Orphan Drug Act of 1983, PDUFA and other healthcare-related legislation.

For these reasons, we appreciate the Committee's continuing interest in our views on user fees, post-market safety of prescription drugs, and the strength of FDA. In addition to its own perspective, NORD plays a leadership role in the FDA Alliance, as well as the Alliance for Drug Safety and Access (ADSA) and will reflect the views of both during this testimony.

We are all aware that confidence in the FDA's judgments on the safety of a wide range of products – from the food on our dinner tables to bestselling, blockbuster drugs, and the latest, breakthrough biotechnology therapies and medical devices – has been greatly shaken. The problems are systemic, cultural and financial. Congress needs to provide FDA with more authority, increased appropriations, and more consistent agency oversight. FDA, an agency that is hardworking and well meaning, needs to remember that regulated industries are “stakeholders,” not customers and that it is the patients and consumers who may live or die and who are most at risk based on the quality and independence of its decisions.

We join others in recommending that Congress enact a PDUFA IV reauthorization in a timely manner well before the current law expires. The reauthorization is necessary and important, but insufficient by itself. NORD believes strongly that Congress has other, equally important tasks to fulfill in an equally timely fashion –

- Strengthen FDA's authorities to assure postmarket drug safety;
- Secure substantial, additional non-user fee appropriations to adequately fund FDA; and,
- Provide consistent oversight to assure the agency's leadership pursues independence and objectivity in its scientific and regulatory operations.

Comments on the PDUFA IV Recommendations, Including Impact on Orphan Product Development

Based on our review of the summary of PDUFA IV enhancements and recommendations, NORD believes that the FDA has secured several important improvements to the existing user fee program. It has omitted other, equally important potential improvements. We would also caution that nothing can be certain about the PDUFA IV recommendations until actual legislative language has been made available to the public and to patients for review.

The PDUFA IV recommendations offer some clear improvements by:

- Allowing FDA to expend user fee revenues for purposes of postmarket risk management and scrutiny of products during the entire duration of their marketing, not restrained by the current limitation of three years post-approval;
- Creating dedicated user fees for the review of voluntary direct-to-consumer (DTC) television advertisements; and,
- Funding of guidance development and the revision of inflation and workload “adjusters” to account for actual submissions and the inflation-adjusted calculation of FDA’s review costs.

NORD’s principal concern with the FDA’s PDUFA IV recommendations is how the program operates in conjunction with the Orphan Drug Act (ODA), which has led to the development and approval of more than 300 drugs and biologics for treatment of rare diseases. Since so much orphan drug development is conducted by small, start-up companies, there is an ever-present risk that user fees (or the perceived burden of user fees) present a potential barrier to innovation, research, product development and market entry.

In particular, we do not want small companies deterred from pursuing promising orphan drug opportunities because modest revenues will be further diminished by product and facility user fees. This is a view that Congress has shared from the beginning of the user fee program and resulted in orphan drugs being totally exempt from application user fees.

The current waiver program administered by FDA for product and facility fees has chosen to interpret gross revenues of \$10 million or greater as evidence that an entity and its affiliates are fully capable of developing and marketing orphan drugs without regard to the cost of users fees. We know that FDA believes that a higher threshold than \$10 million in corporate gross sales will result in a significant expansion of waived products and a noticeable increase in the fees that would be charged to remaining companies. Nonetheless, this does not conform with any common sense view of what constitutes a small company in the bio-pharmaceutical industry and seems unrealistically low, especially with the higher fees that will be required under PDUFA IV.

We come to this issue with a desire to assure that the purposes of both acts be maximized. We do not seek the exemption of all orphan drugs from product and facility user fees, but neither do we feel confident that product and facility user fees are an inconsequential aspect of the development of orphan drugs for small populations or for which there is otherwise modest revenue potential. We seek Congress’ help in resolving this in a way that assures the continued success of the Orphan Drug Act without undercutting the user fee program.

A second principal concern is that the \$37.5 million in user fee funds dedicated to enhancing postmarket safety are inadequate. By comparison, the Institute of Medicine called for \$100 million as a baseline investment in new funds for this purpose. This substantially greater investment in additional user fees and appropriations will be needed to permit the Center for Drug Evaluation and Research (CDER) to:

- Develop, validate, staff, deploy and utilize a wider and ‘smarter’ range of postmarket safety tools and activities;
- Increase staffing in Office of Drug Safety and Office of Surveillance and Epidemiology; and,
- Broaden access to data, employment of new and improved data-mining techniques, and additional epidemiology contracts.

Similarly, we are concerned that the PDUFA IV recommendations only allocate an additional \$4 million for strengthening the information technology infrastructure for drug reviews. This is wholly inadequate given the sadly outmoded and inefficient computer systems upon which CDER relies and the absence of resources to dedicate towards developing uniform standards. While improved IT related to drug safety is a purpose for which appropriated funds should also be requested, we are concerned that what FDA has in mind is a mere drop in the bucket towards the goals of enhancing postmarket safety surveillance and boosting electronic premarket submissions. As a point of reference, patient and consumers groups have been informed that roughly half of the agency’s outmoded IT systems actually can no longer be serviced by commercial vendors. A large investment is clearly needed if IT is to contribute toward improved drug safety at anytime in the next few years.

NORD believes that other resource-starved and otherwise underemphasized enforcement activities need further support. While fees are levied upon submissions, this does not cover the needed level of activity in areas such as facility inspections and FDA’s Bioresearch Monitoring Program (BIMO) inspections. The FDA must shift from reliance upon incomplete, unreliable passive surveillance and the Adverse Event Reporting System (AERS/AERS II) to more directed surveillance and FDA-conducted or mandated observational studies.

Increasing FDA’s Non-User Fee Appropriations is Critical to Protecting Public Health and Advancing Innovation

Like many public and private stakeholders, NORD has been deeply concerned that the FDA does not have adequate resources. We participated in the founding of The FDA Alliance, a broad-based, non-partisan coalition of consumers, patients, health care professionals, and industry, and I serve as a board member and the Alliance’s vice president. With more than 100 members, including seven former FDA Commissioners, the FDA Alliance is an advocate for increased appropriated funding for FDA to enable the agency to effectively carry out its dual roles as a leading guardian of consumer health and safety and as an active leader in advancing global scientific and medical innovation.

As the Senate authorizing committee with jurisdiction over the FDA, we urge the Committee to become activists for FDA funding -- not only through PDUFA and other user fee programs, but through greater, sustained appropriations. This is essential to the agency’s proper functioning as a regulator of food safety, of drug and device safety, and of its critical oversight of the explosive innovation in fields as varied as nanotechnology, molecular diagnostics, pharmacogenomics, and material sciences.

The FDA Alliance specifically asks Congress to appropriate \$2 billion for the FDA in FY 2008, in addition to revenue from user fees. By our calculations, this is the amount needed to restore FDA to its FY 2003 operating level, as well as fund the additional program responsibilities mandated by Congress in subsequent years. This would be an increase of \$450 million over the FY 2007 Continuing Resolution, a large but also prudent and overdue investment in strengthening the FDA, protecting the public health, and enhancing innovation.

As important as this user fee reauthorization is, we cannot emphasize enough how dire the FDA's resource situation has become and how badly the agency is in need of an immediate and substantial infusion of additional appropriated dollars. In short, **PDUFA is a necessary and valuable component of FDA's funding, but it is not sufficient in itself and is simply no substitute for increasing FDA appropriations.**

Leadership is Urgently Needed to Restore Agency Independence and Credibility

Congress and the FDA must also address a third, critical unmet need: sustained leadership that will help the agency shed recent and unwanted blemishes to its "gold standard" reputation for scientific independence and regulatory rigor. NORD has consistently represented to Congress and to the FDA that the agency's success cannot be measured by the speed of its work, but rather the completeness and scientific soundness of its work. I will not belabor the obvious examples of the crises in public confidence suffered lately by the agency, but there is clearly much work to do.

As the Institute of Medicine so forcefully concluded in its September 2006 report, "The Future of Drug Safety":

“[R]ecent highly-publicized controversies ... have contributed to a public perception that the drug safety system is in crisis ... [and q]uestions [have] also surfaced about the independence of the scientific expertise relied on by FDA... and about the possibility of undue industry influence related to CDER's increasing dependence on PDUFA funding...

... Many observe signs of an organizational culture in crisis.”

These are views shared widely among patients, media and regulated industry: that only a strong FDA can sustain – or regain – public confidence in the food, drugs and devices it regulates.

We are encouraged by the Senate's confirmation of Dr. Von Eschenbach, an accomplished clinical scientist and manager, to be Commissioner. We hope that he will steer the agency back towards a more vigorous and timely enforcement of science-based regulatory policy without concession to ideology or politics. We also recommend that Congress undertake two specific tasks to help assure this takes place:

- First, we believe that more consistent and focused oversight by the Committee of the agency's enforcement activities and regulatory policies is needed. We have noted with concern that, over time and certainly since the last PDUFA reauthorization, the agency's responses to congressional requests for information may have become less timely. We consequently encourage the Committee to undertake bipartisan oversight of priority FDA operations through the Committee's investigative staff, sustained communications with agency scientific managers, and the appropriate use of the General Accountability Office and the HHS Inspector General.
- Second, we recommend that the Committee enact revisions to the FDA's statutory mission in the Federal Food, Drug and Cosmetic Act to reflect and reinforce the importance of scientific independence, integrity and objectivity. While this might be dismissed as a gesture, NORD believes that the Commissioner, political managers and career employees alike do or should take heed of the law and of congressional directives in undertaking their duties. That is why we agree with the IOM's recommendation that Congress change the agency's mission statement to further underscore the importance of science, independence, integrity and objectivity.

Enactment of S. 484 Is Needed To Strengthen FDA's Authorities and Better Assure Postmarket Drug

Finally, NORD believes strongly that enactment of S.484, the Enhancing Drug Safety and Innovation Act of 2007, is essential to improve the completeness of FDA's statutory authority, address clear deficiencies in agency practice and culture, and better secure public confidence in FDA's ability to protect the public health. We believe that the bill closely aligns with the Institute of Medicine's recommendations, and that Congress should do no less than what is proposed in the Enzi-Kennedy bill to address the many drug safety crises and failures that have transpired in the recent past.

A. Key Features and Improvements to Postmarket Safety through S. 484

Rather than delve into the specific provisions of S. 484, we believe that the Committee should bear certain key principles in mind when it considers this legislation in the near future. First, the concept of "risk evaluation and management strategy" is based upon well-established FDA regulations, standards and practice. Minimal elements of the proposed "REMS", such as product labeling and adverse drug reaction reporting, are already in place today for all drugs. But the bill builds upon this foundation with essential duties such as required pharmacovigilance, and also provides FDA flexibility to add more requirements, such as patient registries, when called for by the risk-benefit profile of the given drug product.

Because NORD works globally on orphan drug issues, we also believe the Committee should be aware that Europe requires REMS for all drug products in Europe.

We are aware of criticism of the scope and comprehensive reach of the REMS paradigm. But these critics fail or refuse to understand that S. 484 does not require a “one size fits all” application of these safeguards. FDA has historically had great success in applying REMS requirements where the agency has exercised careful scientific judgment about balancing the risks and benefits of their application. First, it is the case that all drug products currently marketed are already held to some or all of the requirements. Second, REMS are particularly useful in challenging cases such as Tysabri, a novel, first-in-class biotechnology therapy for multiple sclerosis, a serious, life threatening disease. FDA’s cooperative employment of appropriate “REMS” controls with the drug sponsor has led to the reintroduction of the therapy in the United States after its voluntary market withdrawal.

It is within the REMS paradigm that S. 484 also endows FDA with the critically important authorities to require post market studies and to compel labeling changes to reflect new safety information when sponsors fail to act in a timely or appropriate manner. The legislation also creates a publicly accessible registry of clinical trials and clinical trial results. These are vital changes to FDA authority that must be enacted to address past failings, to close loopholes in the law, and to secure patient access to safe and effective drugs and the information needed to use them.

B. Potential Enhancements to S. 484

There are enhancements to S. 484 that NORD believes could strengthen its already important provisions. First, NORD believes that the Dodd-Grassley Fair Access to Clinical Trials (FACT) Act of 2007 offers superior features in the organization and implementation of a clinical trial registry and disclosure database. Second, minor enhancements to the Kennedy-Enzi REMS paradigm are possible, such as omitting exceptions for current sponsor-controlled labeling changes to ensure FDA remains the ultimate arbiter of safety-related drug labeling. And finally and most importantly, NORD believes that S. 484 can provide for additional mechanisms to assure patient and provider input in the development of REMS plans – and the features of future PDUFA reauthorizations.

Conclusion

Rare disease patients are no different from most patients in their views and concerns about drug safety. We want innovative medicines as quickly as they can be tested, evaluated, proven, approved, and marketed. We can accept certain risks in new medications, if they are properly considered by FDA, accurately labeled by the sponsor, and correctly prescribed by health care professionals.

Safety can never be absolute, which is exactly why patients are so dependent on the thoroughness and competency of FDA’s review process and why FDA needs additional authority to oversee and act during the post-market period. Patients depend on the industry’s skill in innovation and product development, but will necessarily be cautious without the assurance that FDA has thoroughly evaluated the safety and effectiveness of new therapies.

Although I cannot speak for industry, the credibility of FDA's review process should be every bit as important to them. Public confidence in FDA translates into patient and prescriber confidence in FDA-approved therapies. A strong FDA review process increases the value of approved products from both the patient and company perspective.

Seen this way, passage of S. 484 is a matter of urgency and one which benefits all stakeholders. Conversely, failure to enact S. 484 risks a repeat of the uneven and often disastrous safety decisions that have led to drug withdrawals, questionable sponsor practices, and apparent regulatory failures that have so badly eroded public confidence in FDA – and by extension in the safety and effectiveness of drug therapies.

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