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ON BEHALF OF THE PATIENT AND CONSUMER COALITION
BEFORE THE SUBCOMMITTEE ON HEALTH
OF THE HOUSE ENERGY AND COMMERCE COMMITTEE
REGARDING THE EFFECTIVENESS OF THE FOOD AND DRUG ADMINISTRATION MODERNIZATION ACT
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Good morning. I am Travis Plunkett and I serve as the Legislative Director of the Consumer Federation of America. I am here today on behalf the Patient and Consumer Coalition, an ad hoc coalition of patient and consumer advocacy organizations working to insure greater access to safe, effective affordable drugs and medical devices. The coalition also focuses on enhancing the ability of the Food and Drug Administration to protect public health through effective enforcement of the law. (Please see the attached for the coalition's mission statement and founding members.) This testimony is endorsed by the following members of the coalition: Center for Medical Consumers, Consumer Federation of America, Gay Men's Health Crisis, National Consumers League, National Organization for Rare Disorders, National Women's Health Network, Public Citizen, UAW and the U.S. Public Interest Research Group.

I would like to thank Chairman Bilirakis and Ranking Member Brown for the opportunity to offer comments on the impact of the Food and Drug Administration Modernization Act (FDAMA) on consumers and patients nationwide. We urge the subcommittee and the full committee to have several hearings to evaluate both the impact of FDAMA on public health and safety, as well as the range of possible changes that could improve it. I will focus my comments on a key component of the Act: the expansion of the Prescription Drug User Fee Act (PDUFA.) I will also comment briefly on the "pediatric exclusivity" provision that grants additional patent life to drug manufacturers that conduct clinical tests on the effect of their drugs on children.

<u>The Prescription Drug User Fee Act</u>

As you know, PDUFA was first enacted in 1992 to address concerns about the length of time it took for new drugs to treat life threatening and disabling conditions to be reviewed and approved by the FDA. While the issue of new drug approval time had been a contentious one for several decades, the experience with HIV/AIDS convinced many that there was room for improvement. PDUFA recognized the reality that the resources of the agency were constrained

and that a shorter approval process would require considerably more staff devoted to the drug review process. User fees were imposed upon industry that would fund the additional agency resources needed to speed up the review and approval process.

PDUFA was reauthorized in 1997 as part of the FDAMA. However, this iteration introduced increasingly stringent “performance goals” requiring that the FDA meet tight review deadlines. It even includes stipulated time frames for scheduling of meetings and response to industry requests. For example, the 1997 PDUFA establishes a performance target that requires FDA to review 90 percent of priority new drug applications within 180 days and non-priority new drug applications with 10 months. These mandates were insisted upon by the industry that argued that these “measurables” were necessary to ensure that the user fees they paid were not dispersed to fund other agency activities.

As a result of the 1992 and 1997 legislation, the FDA has dramatically increased the amount of resources it devotes to new drug and biologics review and approval from $120 million in 1992 to a projected $325 million in FY 2002. In FY 2002, it is estimated that a record half of the resources required for new drug approvals will come from user fees paid by the regulated industry.[1]

Has PDUFA been a success? Well, if success is only measured by the goals mandated in 1997, the answer is a resounding “yes.” The time for approval has decreased from a median of slightly less than two years in 1992 to less than one year at present. A higher percentage of applications are now approved; 80 percent compared with only 60 percent in 1992.[2]

But the success of a drug review and approval process should not be measured by speed and approval rates alone. The FDA’s responsibility under law is to ensure that new drugs and devices are safe and effective. That is the true public health responsibility of the agency by which its success or failure must ultimately be measured. We believe that the effect of PDUFA II on public health and safety is a matter for grave concern.

1. PDUFA creates a financial dependence by the FDA on an industry it regulates. This is a conflict-of-interest that could compromise drug safety. Our organizations recognize that PDUFA has provided the agency with the resources to speed up new drug approvals since 1993. Clearly there are public health benefits to be gained from faster approval of <u>certain</u> new drugs. These include medications that treat serious and life-threatening conditions, drugs that provide

relief for patients with illness or disability refractory to existing therapies, or drugs that are less toxic than currently available therapies.

However, the FDA's direct fiscal interest in optimizing user fee income to achieve speedier approval times and get more drugs through the approval process in each budget year creates an obvious tension with its responsibility to assure the highest degree of safety and efficacy of new products. As mentioned above, the FDA's dependency on fees paid by the regulated industry has grown dramatically since fees were first initiated in 1993. The integrity of the drug approval process is what is potentially at risk and, as a result, the safety of the millions of Americans who use prescription drugs could be compromised.

The growing number of recalls and warnings related to newly approved drugs has reinforced our concerns. The agency has attempted to demonstrate that there is no relationship between faster approval times and more frequent recalls or additional safety warnings. However, there have been too many recent withdrawals of marketed drugs that have killed and injured people that have cast a serious shadow over the integrity of the approval process. Eleven prescription drugs have been pulled from the U.S. market in the last three and one-half years for safety reasons, by far the most such actions taken in any comparable period. More than 22 million Americans took those drugs. Just last week, the anesthetic Raplon was removed from the market, after five people were reported to have died from bronchospasm.

These eleven drugs include three that were approved before PDUFA took effect in 1993, but the withdrawn drugs Lotronex, Propulsid, Rezulin, Raxar, Posicor, Duract and Redux have all been approved since 1993. According to the Pulitzer Prize-winning investigation by David Willman of the *Los Angeles Times*, these seven drugs are suspected in 1,002 deaths. [3] This is based on the FDA's reporting of "adverse events," which doesn't prove that a particular drug caused a death; it is merely a "primary suspect." However, adverse events reports are also voluntary, so the true number of fatalities caused by these drugs could be much higher. Adverse events reported to the FDA increased by 89 percent from 1993 to 2000.[4]

Moreover, we are particularly concerned that, to date, the risks posed by these drugs have fallen disproportionately on women. In January, the U.S. General Accounting Office (GAO) reported to Congress on the subject of drug safety with the significant finding that most drugs withdrawn in recent years had greater health risks for women. Specifically, the GAO

investigation found that, “Eight of the ten prescription drugs [withdrawn from the U.S. market since January 1, 1997] posed greater health risks for women than for men” and that four of the drugs withdrawn “had more adverse events in women even though they were widely prescribed to both women and men.”

Only one of the drugs withdrawn from the market since 1993, the antibiotic Raxar, had lifesaving potential. It was ultimately determined to be unnecessary because other, safer antibiotics were available. Willman’s investigation also included reports from a number of former FDA employees that the need to act quickly--as required by PDUFA--and the demands of FDA officials, put them under enormous pressure to approve new drug applications, whether they felt the drugs were safe or not.

As if to confirm our fears, the term “customer” has crept into the FDA’s characterization of the prescription drug industry. We are very concerned that an agency chartered to safeguard the public’s health would characterize the industry it regulates as its primary customer, and itself as a “supplier” of services (namely new drug review and approval.) It is the public, not the drug industry, that should be the FDA’s “customer.” The medical and public health consequences of faster drug approval are the appropriate measure of PDUFA’s successes and failures, not the tabulation of the average number of months a drug requires for approval.

2. PDUFA’s performance goals are inappropriate, potentially dangerous and open to manipulation by the drug industry. Although the FDA takes pains to explain that the performance goals mandated under PDUFA are for decision-making, not approval, these goals put the FDA under tremendous financial pressure to move very quickly on the overall approval process. Here’s what William B. Schultz, a former deputy commissioner at the FDA told the *Los Angeles Times* about PDUFA deadlines: “You can meet the goal by either approving the drug or denying the approval. But there are some who argue that what Congress really wanted was not just decisions, but approvals. That is what gets dangerous.” Dr. Solomon Sobel, the former director of the FDA’s metabolic and endocrine drugs division told the *Los Angeles Times* that deadline pressure under PDUFA was not just to make decisions: “The pressure to meet deadlines is enormous. The basic message is to approve.”[5]

These goals force the agency to take an unvarying, “cookie cutter” approach to drug approvals. It is not in the public interest to require the FDA to act at the same speed for all

standard or priority drugs and biologics. Some should get more time, some should receive less; time should not be the measurement of the agency's success. The agency has adequate tools to enable patients to obtain drugs before they are approved for marketing (as with the Treatment IND), so that desperately ill patients can have early access to potentially important medicines.

Moreover, it is completely inappropriate to give a regulated industry a dominant voice in determining what will be the process ("performance goals") for oversight of that industry. Congress established these goals in consultation with the prescription drug industry and received absolutely no input from consumers. The end result is that the regulated industry controls not only the funding and timeline for new drug approval, but the measurement tools that are used to determine the FDA's success or failure in this matter.

PDUFA allows companies to manipulate the FDA into quickly approving drugs that the agency has not had adequate time to review. Companies can do this simply by dragging their feet in submitting required data and test results until the FDA's "performance" deadline draws closer. If this practice is used on a regular basis, it puts the FDA under tremendous time pressure to meet its performance goals without adequately reviewing the submitted data. In other words, the FDA's performance goals, which are based on the agency's ability to meet many decision-making deadlines over the course of time, may actually provide companies with an incentive to delay transmitting some data to the FDA quickly. If they give the FDA the information "too early," the agency might actually have more time to find flaws in the information.

3. PDUFA is draining resources from other critically important FDA public health functions, such as monitoring the safety of drugs once they are on the market and approving generic drugs for entry into the market. This distorts the overall priorities of the agency. The pharmaceutical industry insisted that a large, inflation-adjusted portion of drug review costs be funded through appropriations. Congressional budget increases to the FDA have not kept up with the mandated spending increases in PDUFA. According to the FDA, it has had to absorb $284 million in unfunded pay raises and other inflationary costs in the last eight years.[6] To his credit, the President has proposed funding in his budget to catch-up on these expenses.

Here's what the FDA has to say about the impact of PDUFA on the rest of their mission: "We are increasingly concerned that spending enough appropriations on the drug review process to meet the statutory conditions makes the FDA less able to manage the resources available in a

way that best protects the public health and merits public confidence."[7] Former Commissioner Jane Henney went a step further, "…the truth is, the program is barely surviving because of the way it was designed. We don't have the resources to do the things we believe are essential, such as adverse event reporting, because they are not supported by PDUFA funds."[8]

Moreover, the director of FDA's Center for Drug Evaluation and Research, Janet Woodcock, has expressed a great deal of concern about FDA staff turnover, and ultimately, their experience and competency. She has said that the intense timelines under PDUFA have created a "sweatshop environment that's causing high staffing turnover."[9] Many of the FDA's most highly trained scientists and experts are leaving within three years, preventing the agency from building an institutional memory of previous reviews.

One of the areas of FDA's work that is suffering from a dramatic lack of resources in the post-FDAMA and -PDUFA era is oversight of prescription drug advertising to consumers. As the number of drugs approved has increased, so has industry spending to promote these drugs. Since 1997, pharmaceutical industry spending on direct-to-consumer advertising has skyrocketed: increasing by 42 percent between 1996 and 1997, by 23 percent between 1997 and 1998, and by 40 percent between 1998 and 1999. In 1999, drug companies spent more than $1.8 billion on direct-to-consumer advertising.

The FDA staff responsible for reviewing these promotional materials has not increased proportionately. FDA has only 13 people responsible for primary review of the 32,000 pieces of promotional material that the agency receives in a year. This level of resource commitment is clearly insufficient to enable FDA to act promptly on violations of the requirement that ads be accurate and include a fair balance of information about risks as well as benefits. Slow action on inaccurate and incomplete advertisements is a serious problem for consumers. Until the agency informs a company that it must withdraw or change an ad, the public will continue to be exposed to false information and to ads that fail to include important risk information. Delays in this area pose an unacceptable threat to the public health.

4. PDUFA does not prioritize between speedy approval of drugs that are truly important and those that represent no therapeutic advancement. Unfortunately, the FDA's regulatory process as defined by statute and regulation does not provide it the latitude to prioritize the new drug approval process based on a ranking of medical and public health needs. The FDA has four

categories for approval of new drugs: (1) Those for serious or life-threatening conditions for which there is no adequate treatment; (2) drugs for rare disorders; (3) the majority of new drugs that are approved, which are redundant chemical modification of drugs already marketed; and (4) drugs that are granted priority review because they work in some new way.

We suggest that drugs that fall into the third category above, such as a drug for erectile dysfunction, or the third or fourth cox-2 inhibitor, do not need to be rushed to market as quickly as an important new anti-cancer agent or an enzyme replacement therapy for a genetic disease. Many new drugs that have appeared on the market as a result of the agency's PDUFA enhanced approval resources, may actually turn out to provide little, if any, benefit to patients when compared to older, better-understood and often less expensive predecessor drugs.

5. The best way to insure the timely approval of safe drugs is to adequately fund the FDA from general revenues. Adherence to this principle would be the surest way to remove the worrisome potential for conflict-of-interest that arises when dedicated income streams flow to the regulator from the regulated industry. If Congress continues to underfund the FDA, it will be essential for Congress and the agency to establish better procedures and guidelines to prevent the serious conflict-of-interest concerns that our organizations have raised in this testimony.

Pediatric Exclusivity

FDAMA granted drug companies a six-month patent extension if they conduct pediatric testing on a particular drug. This provision expires in January of next year. The Patient and Consumer Coalition agrees with the FDA that the pediatric exclusivity provision "has been highly effective in generating pediatric studies on many drugs and in providing useful new information in product labeling."[10] As a result, we support renewing this provision.

However, Congress should enact measures to make pediatric exclusivity more targeted and effective. Pediatric exclusivity has delayed the introduction of more affordable generic alternatives on some very important and widely used drugs and has proven to be very lucrative for brand drug companies. But it has not yet resulted in the testing and labeling of some of the most widely used pediatric drugs. Six of the ten drugs without adequate labeling for children are not eligible for pediatric exclusivity because they are off-patent. For example, dopamine hydrochloride, which is used to stabilize the blood pressure of sick babies, has never been formally tested in children. Moreover, the exclusivity applies to every formulation of a drug,

even if only one formulation is tested.

We recommend that Congress consider a number of possible measures that could make pediatric exclusivity more effective and less costly, while still providing an incentive for brand companies to test. Our coalition has not formally endorsed any of these proposals yet, but we urge Congress, as we are, to seriously consider each of them. These measures could include: tax credits to encourage companies to conduct studies on drugs that are off-patent; making funds available to the Centers for Education and Research on Therapeutics (CERT) sites and the Pediatric Pharmacology Research Units to do testing of drugs that are off-patent; allowing exclusivity only on the particular formulation of a drug that is tested, and not on others in that line that will not be offered to children; scaling the length of exclusivity to the sales of a drug, so that Americans would not have to pay higher prices on blockbuster drugs that recoup the cost of pediatric testing in far less than six months; directly linking the granting of exclusivity to a company making labeling changes, and codifying the FDA's authority to require companies to test new drugs on children. Congress should also insist that the FDA retain bioethicists to review all proposed pediatric clinical trials in order to ensure that the agency gives appropriate consideration to the ethical concerns that come up around the possibility of exposing children to unnecessary and sometimes dangerous risks in clinical trials.

In conclusion, let me say that Congress will consider no legislation this year that is more important to this nation's safety and health. As a result of the serious problems that I have noted with the Prescription Drug User Fee Act, what is at stake is nothing less than public trust in the nation's drug safety system. Right now, Americans have every reason to wonder if the FDA can really protect them. We urge this committee to act quickly to eliminate conflicts-of-interest in PDUFA, prevent the drug industry from dictating the timeline and standards for drug approval and properly fund all FDA drug monitoring and approval functions—not just new drug approval. It is time to refocus the FDA's attention on its real customers: the American people.

Thank you again for the opportunity to offer our comments.

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[1] Food and Drug Administration, "PDUFA Background Information," August 2000.
[2] Ibid.
[3] David Willman, "How a New Policy Let to Seven Deadly Drugs," *Los Angeles Times*, December 20, 2000.
[4] Ibid. Adverse events increased from 136,836 in 1993 to 258,125 in 1999.
[5] Ibid.
[6] FDA Talk Paper, April 9, 2001
[7] Food and Drug Administration, "PDUFA Background Information," FDA, August 2000.
[8] FDA Consumer Magazine, "User Fees for Faster Drug Review: Are They Helping or Hurting the Public Health?," September-October 2000.
[9] Ibid.
[10] Department of Health and Human Services, U.S. Food and Drug Administration, "The Pediatric Exclusivity Provision, January 2001, Status Report to Congress."