Consumer Federation of America

COMMENTS OF TRAVIS B. PLUNKETT, LEGISLATIVE DIRECTOR ON REAUTHORIZATION OF THE PRESCRIPTION DRUG USER FEE ACT BEFORE THE FOOD AND DRUG ADMINISTRATION PUBLIC MEETING DECEMBER 7, 2001

Good morning. I am Travis Plunkett and I serve as the Legislative Director of the Consumer Federation of America. CFA is an association of more than 280 organizations that, since 1968, has focused on consumer education and advocacy. We have worked for many years to improve consumer access to safe, affordable prescription drugs and to enhance the ability of the Food and Drug Administration to protect public health. CFA worked closely with the Patient and Consumer Coalition as part of the debate on the renewal of PDUFA and enactment of the Food and Drug Administration Modernization Act in 1997. We are also a member of a coalition of business, insurer and consumer organizations, RxHealth Value.

I would like to applaud the FDA for its consistent efforts over the last year to reach out to the public and to consumer and patient groups about reauthorization of PDUFA next year. This law is vitally important to public health and safety and we appreciate your efforts to solicit input about PDUFA from the people whose health and safety is most directly affected by it: patients and consumers.

A. BACKGROUND ON PDUFA

As you know, PDUFA was first enacted in 1992 to address concerns about the length of time it took for new drugs treating 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 drug review. 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

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deadlines. 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 within 10 months. These mandates were insisted upon by the pharmaceutical industry, which argued that these "measurables" were necessary to ensure that the user fees they paid were not dispersed to fund other agency activities. For the first time, it included stipulated time frames for scheduling of meetings and response to industry requests.

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 $329 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]

B. HAS PDUFA SUPPORTED THE FDA'S MISSION TO PROTECT AND PROMOTE PUBLIC HEALTH?

If success is only measured by the goals mandated in the 1997 act, the answer is a resounding "yes." The time for approval of new drugs declined from a median of slightly less than two years in 1992 to less than one year in 2000.[2] Approval time is now about 15 months. A higher percentage of new drug applications are now approved as well; 80 percent compared with only 60 percent in 1992.[3]

Clearly there are very important public health benefits to be gained from faster approval of certain 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.

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 obviously 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.

If success is measured by a balanced assessment of both the advantages and disadvantages of faster new drug approval—such as the negative public health effects of drugs that have harmed or killed Americans and have subsequently been withdrawn from the market—there is definitely cause for concern, and for further investigation. And if success is measured by the draining effect of PDUFA on the FDA's ability to achieve the rest of its public health

mission—a fact that the FDA has openly acknowledged--then one can only deduce that PDUFA has not provided a net benefit to the public health. CFA has come to this conclusion for the following reasons:

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. 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 withdrawals of marketed drugs that have killed and injured people that have cast a serious shadow over the integrity of the approval process. Twelve prescription drugs have been pulled from the U.S. market in the last four years for safety reasons, by far the most such actions taken in any comparable period. Only three of these withdrawn drugs were approved before PDUFA took effect in 1993. The most recent withdrawal was the anti-cholesterol drug Baycol, which is implicated in 31 deaths. More than 22 million Americans took the drugs that were withdrawn prior to Baycol.

According to the Pulitzer Prize-winning investigation by David Willman of the *Los Angeles Times*, seven of these drugs-- Lotronex, Propulsid, Rezulin, Raxar, Posicor, Duract and Redux--are suspected in 1,002 deaths. [4] 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 suspected. 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.[5]

Only two of the drugs withdrawn from the market since 1993, the antibiotic Raxar and Baycol, had lifesaving potential. Raxar 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."

2. PDUFA's performance goals are inappropriate and potentially dangerous. 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."[6]

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.

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.[7] To their credit, the President proposed and Congress approved appropriations for FY 2002 to catch-up on these expenses. The budget includes $45 million for cost-of-living salary increases, $10 million for post-marketing surveillance of drug safety, $10 million for infrastructure improvement and $2.5 million for approval of generic drugs. The speed of generic drug approval actually lags behind that of new drugs, at an average of 18 months. These intial funding increases are a step in the right direction but the President and Congress will have to do far more to adequately fund the FDA's public health mission.

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."[8] 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."[9]

Moreover, the director of FDA's Center for Drug Evaluation and Research, Dr. 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."[10] 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.

C. WHAT SHOULD BE RETAINED OR CHANGED TO ENHANCE THE PROGRAM?

1. 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. Moreover, as I mentioned before, Congress should also provide additional appropriations for public health functions that are suffering, including

post-marketing surveillance, adverse event reporting, generic drug approval, direct to consumer advertising and food safety. If Congress continues to underfund the FDA, it will be essential for the agency to establish better procedures and guidelines to prevent the serious conflict-of-interest concerns that our organizations have raised in this testimony.

2. Regulated interests should not be allowed to inappropriately influence FDA functions through the use of new user fees. If an unwillingness to appropriate adequate funds leads Congress to consider the expansion of new user fees, it is absolutely essential that a "firewall" be placed between the disbursement of user fees and the performance by the FDA of its mandated responsibilities. State utility commissions and insurance departments often assess regulated businesses for the cost of oversight. Although conflicts-of-interest sometimes occur at these agencies, this approach gives the regulated industry far less control over the priorities of the agency and the manner in which success or failure is measured than a dedicated funding stream like PDUFA user fees.

3. PDUFA's performance goals should be overhauled. There is absolutely nothing wrong with a federal agency using performance goals as an internal management tool to achieve its public health goals, hold its employees accountable to measurable standards and better serve the public. However, as I've already pointed out, the performance goals in PDUFA II have become far more than a management tool. They have given a regulated industry inappropriate and potentially dangerous control over the functions of the regulator.

Performance goals that are included in PDUFA III should be consistent with three important principles. **First, public health should be the paramount concern.** Medical officers and FDA scientists—not one-size-fits-all-deadlines that are rigidly interpreted—should determine the speed of new drug approval. Moreover, Congress should construct a series of rational, specific public health performance goals that the FDA should be required to meet.

Secondly, the FDA must be given meaningful flexibility to implement the performance goals. Congress should stop micro-managing the agency and lengthen decision-making deadlines or write an "override" clause into the statute. Such an approach would give scientists and medical officers the right to slow down the approval process for any application if public health concerns exist, without facing censure by the agency. **And finally, PDUFA should allow for greater differentiation within the standard and priority review categories.** This would allow the agency to put the approval of drugs that are not breakthrough or lifesaving therapies on the "back burner" if conditions warrant.

Thank you for the opportunity to offer CFA's comments on this important topic. Congress will consider no legislation next year that is more important to this nation's safety and health. As a result of the serious concerns with the Prescription Drug User Fee Act that I have noted, what is at stake is nothing less than public trust in the nation's drug safety system. We look forward to working with you to achieve passage of legislation in 2002 that allows the FDA to focus its attention on its real customers: the American people.

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[1] Food and Drug Administration, "PDUFA Background Information," August 2000.
[2] Ibid.
[3] Federal Register;Vol. 66, No. 223/; November 19, 2001; Docket No. 01N-0450.
[4] David Willman, "How a New Policy Let to Seven Deadly Drugs," *Los Angeles Times*, December 20, 2000.
[5] Ibid. Adverse events increased from 136,836 in 1993 to 258,125 in 1999.
[6] Ibid.
[7] FDA Talk Paper, April 9, 2001
[8] Food and Drug Administration, "PDUFA Background Information," FDA, August 2000.
[9] FDA Consumer Magazine, "User Fees for Faster Drug Review: Are They Helping or Hurting the Public Health?," September-October 2000.
[10] Ibid.