Statement of Consumers Union
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November 14, 2005

PDUFA IV: Putting the Public Health First

An Opportunity to Ensure Safety and Effectiveness are Prioritized in the Drug Approval Process

Mr. Chairman, Members of the Committee:

On behalf of Consumers Union, the independent, non-profit publisher of *Consumer Reports*, we urge the FDA to use the opportunity of PDUFA extension to seek fundamental legislative reforms in the agency:

- to continue to bring increased emphasis to safety, and
- help the American public understand what medical treatments are truly effective.

Response to FDA Questions

The FDA posed some important questions in calling this meeting, most notably, asking for an assessment of the overall performance of PDUFA to date.

While there are some benefits resulting from the agency getting increased funds to speed review of new, life-saving drugs, we believe the overall result of PDUFA has been to undercut the independence and objectivity of the agency due to its reliance on industry funding. In turn, this undercuts public trust in the FDA's primary mission of protecting our nation's health and welfare. By shifting resources to speeding drug approval without a concomitant increase in drug safety, PDUFA has created a lopsided agenda in the agency that, in part, has resulted in the kinds of drug safety tragedies we've seen play out over the last several years.

On the question, "What aspects of PDUFA should be retained, or what should be changed to further strengthen and improve the program?" we believe that when PDUFA is extended:

- Collected fees must be decoupled from specific pre- and post-performance goals that have been rushing the approval of unsafe drugs and limiting follow-up safety efforts;
- A much larger level of income should be collected, since the amounts provided in PDUFA III have been completely inadequate to fulfill the overall mission of the FDA.
- Much of the increase should be used by the agency to improve post-approval monitoring and safety, conduct prior review of marketing materials, and ensure that safety studies are completed to help consumers fully understand the comparative value of approved drugs.

Creating an Effective FDA that Serves the Public

Extending PDUFA is not our first choice for creating an agency that truly serves the public. We believe that most Federal agencies carrying out the public's business should be funded by the general Treasury to avoid conflicts of interest.

As such, we support the legislation proposed by Representatives Hinchey, DeLauro, and Stupak[1] that would designate that PDUFA user fees be deposited into the general Treasury and that amount transferred to the FDA as mandatory spending, with no strings attached. The bill also includes sections very similar to S. 930, the Grassley-Dodd legislation that we have endorsed, creating a separate Office of Drug Safety that is appropriately funded, with clearer authority (including use of Civil Monetary Penalties) to require post-approval safety studies that actually get completed, prior review of DTC ads, immediate adjustment of warning labels, and risk management programs.

We believe that these types of safety authorities, along with the reforms contained in S. 470 that would ensure a publicly accessible clinical drug trial database, would result in a much safer world of prescription drugs, without slowing the approval process or keeping life-saving and life-improving drugs from patients. While some of these measures may take additional resources, they will fulfill the agency's mission by ensuring safety and research have an equal place at the drug-approval table.

Why PDUFA is a Problem

There is an ancient folk wisdom, that "he who pays the piper, calls the tune." PDUFA fosters a public notion that the FDA is too friendly with the very industry it is supposed to regulate because it pays half the salaries in the Center for Drug Evaluation and Research. As has been reported, some in the FDA have referred to the drug industry as 'clients.' PDUFA money, tied to intricate guidelines on how it is to be used, timetables, and meeting schedules, is driving the agency. As the September 2002 GAO report[2] on the effect of user fees noted, the process has created real problems with employee retention and morale.

The very process in PDUFA III to prepare for PDUFA IV proves the point: Section 505(a)(1) of PDUFA III calls for 'consultation' with Congress, academics, consumers, and the regulated industry. That is the process we are going through today. But the very next section (a)(2) provides for the FDA to make its recommendations, "after negotiations with the regulated industry."

While the "consultation" with consumers is a welcome change from previous practice, provisions allowing the industry to "negotiate" FDA recommendations undercuts the agency's true role as an independent, drug safety regulator. If the FDA — and the pharmaceutical industry — are going to regain the respect and trust of the American public, the FDA must be

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[1] HR 2090, 109th Congress.

[2] GAO-02-958, "Effect of User Fees on Drug Approval Times, Withdrawals, and Other Agency Activities."

seen as an objective arbiter with a clear mission to serve the public, and its reliance on the goodwill of the industry they are supposed to oversee must end.

The Need for More Resources

We realize it is unrealistic to expect that if PDUFA expires, the Congress will make up the difference out of general revenues. Without PDUFA's resources, it is hard to imagine how the FDA would function.

We believe the FDA needs more resources to serve the public appropriately. We urge that the level of user fees be substantially increased, but without conditions that tie FDA management to serving the industry rather than the public.

The industry is best served by a drug approval and monitoring system that the public trusts. By helping to adequately fund the FDA, the industry will be able to begin recovering that vital trust.

1. <u>We need more resources to ensure the safety of drugs and devices in the marketplace</u>.

It is clear that some drugs with unacceptable safety risks are being approved.[3] Tens of thousands of people have died and been injured under the current system, which emphasizes getting drugs to market, while giving short shrift to determining the safety of those drugs once they are in the marketplace and in use by millions of Americans.

The October 25 decision of the FDA Advisory Panel on psychiatric drugs illustrates this problem: rather than slow the entry of new drugs by requiring more comprehensive testing, the panel wanted (and the FDA appears to be agreeing) almost immediate approval. The result will be the marketing of more drugs that we do not fully understand and that may have higher risks (and fewer benefits) than we can detect in short trials.

Balancing quick access to life-saving drugs with safety and affordability is not a simple task, but it should be the FDA's primary goal. To reach this, the FDA must give as much organizational attention and resources to safety and post-approval studies as it gives to speeding up the approval of new drugs. It also will require acknowledging that during the two or three years after a drug is approved and marketed, vital information is lacking on both its effectiveness

[3] While the final approval decision is unclear, the failure of the Advisory Committee process (and of the FDA to highlight problems for the Advisory Committee) in the recent Muraglitazar/Pargulva review is just one more example of on-going problems. Even when a safety problem is detected, the response can be inadequate from a consumer standpoint. For example, in October, 2005, in the case of pemoline (Cylert) with its unacceptable liver toxicity problem, remaining supplies will be allowed to be sold, rather than recalled and destroyed. We hope there will be no "final clearance" ads for this drug! We urge that the FDA consider the points raised by Doctors Hayward, Kent, Vijan and Hofer, in their November/December 2005 <u>Health Affairs</u> article, "Reporting Clinical Trial Results To Inform Providers, Payers, and Consumers." The article points out that "the conventional approach to reporting clinical trials has fundamental flaws that can result in overlooking identifiable subgroups harmed by a treatment while underestimating benefits to others."

and safety. This fact has long been recognized, but only in the last five to 10 years has it become urgent as more drugs for chronic illness have become available and their use exploded. Today, tens of millions of Americans take two to three or more drugs every day, day-in and day-out, for years.

The only way to mitigate the damage of quick approval of drugs tested on a small population base is to prohibit widespread advertising for the first two to three years after a drug has been approved. Two-thirds of all drug withdrawals occur within the first three years of release, so a three-year moratorium would result in a major reduction in the use of drugs eventually found unacceptably risky.[4] Therefore as part of overall safety improvements, we support Senator Frist's call for a two-year moratorium on drug advertising. We support Rep. Sherrod Brown's bill (HR 3696) for a two-year moratorium, and Representatives Jo Ann Emerson and Rosa DeLauro's proposal for a three-year ban (HR 3950).

In addition to a moratorium on mass advertising of new drugs, the FDA needs the resources to require the completion of post-approval safety tests. Today, companies give a commitment, but too many fail to keep it in a timely manner. The FDA needs the staff, resources and legal authority to impose civil monetary penalties to force the completion of these studies.

We also are concerned about the recent press stories on the Guidant heart devices and the delay in public reporting of life-threatening defects. While it seems a simple matter to require a change in manufacturer filings so as to make safety issues stand out in neon lights, it also appears that the staff resources were lacking to read the company's filings in a timely manner. User fee revenues can help with this type of basic resource need.

2. The FDA needs resources for the aggressive use of new databases to detect long-term safety problems.

The current adverse event reporting system can be useful at times for detecting unusual and rare events, and certainly the resources should be made available to review all serious reports within a 15-day period. But the advent of large new databases, from private insurers and especially the Medicare prescription drug database, gives us the potential to detect problems with drugs and drug interactions much earlier and in a much more scientifically robust way. To date, we have not heard details or received assurances that this new resource will be fully used. One recent news report indicated that the Health Information Technology and Electronic Medical Record movement might have a system in place by 2014 that would 'spot emerging evidence of drug hazards.'[5] The FDA must be prepared to receive and use these data bases, and ensure that CMS is providing the appropriate data fields. This point was made by Dr. Scott Gottlieb in his July/August 2005 Health Affairs article, "Opening Pandora's Pillbox: Using Modern Information Tools to Improve Drug Safety." Some dedicated resources need to be given to this project, since the nine-year delay in implementation cited in the article is far too long.

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[4] Matthew F. Hollon, MD., "Direct-to-Consumer Advertising: A Haphazard Approach to Health Promotion," JAMA, April 27, 2005. Vol. 293, No. 16, p. 2032.

[5] Healthbeat, October 26, 2005, "Federal Advisory Panel: Privacy Safeguards Are Key to Advance of Health Care IT."

3. Given the long history of marketing violations, the FDA needs the resources to review all marketing materials before they are distributed to providers and the public.

Consumers Union has been working on the issue of drug ads for a long time, with a June 1996 report and a February 2003 report entitled, *"Free Rein for Drug Ads? A slowdown in FDA review has left consumers more vulnerable to misleading messages."* This report details our analysis of FDA regulatory letters relating to ads, both direct-to-providers and direct-to-consumers (DTC), issued between January 1997 and November 2002.[6] We found:

> a broad and disconcerting range of misleading messages: ads that minimized the product's risk…; exaggerated its efficacy; made false claims of superiority over competing products; promoted unapproved uses for an approved drug; or promoted use of a drug still in the experimental stage.

A reading of recent regulatory letters seems to indicate a welcome up-turn in strong warning letters, for which we congratulate the FDA. We particularly appreciate the emphasis on ensuring that the risks of a drug are given more prominence.[7] But it appears that the overall level of policing of promotions is still down from the previous decade — and that nothing has changed in the type of abuses detected.

Companies are repeatedly warned about similar violations, all too often after the ad campaign has ended and the public damage done. In our 2003 report, we noted how the maker of Claritin had received a total of 11 regulatory letters about problems with their ads. With these kinds of repeat warnings, one gets the strong impression that many in the industry are just scoffing at the requirements, or as someone has said, 'the FDA is just playing a game of whack a mole,' as it tries to stop DTC and DPC abuses.

This disregard for the rules and regulations is why the law should be changed to permit imposition of major civil monetary penalties (CMPs) for violations, especially repeat violations.

Since the industry has so consistently failed to comply with the rules and regulations, we urge that FDA review and pre-clearance of all direct-to-consumer and direct-to-physician advertising be required. If the FDA decides not to proceed with this recommendation, it should require corrective ads and take other enforcement action (and seek CMP authority) for any violations of truth and accuracy. That will take additional resources.

We also support legislation by Senators Grassley and Dodd (S. 930) that would, among a number of important safety provisions, require pre-review of advertising materials for all drugs for which postmarket study requirements have not been fulfilled, and require enhanced disclosures to the public about the safety uncertainties that may accompany the drug.[8] Not only

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[6] We will be updating this study in the next few months.

[7] The Pink Sheet, August 1, 2005, "FDA Ad Division Letter Shows Focus on Prominence of Risk Information. P. 7.

[8] We also have endorsed the provision in S. 930 that would require review of advertising and promotional materials for new drugs for the first two years after approval and require improved risk communication to consumers in those materials. But as stated earlier, we also strongly support the much stronger proposal to prohibit such ads for the first two or three years a drug is on the market.

would this provision help consumers understand the possible risks of a drug, but it would be a major incentive to manufacturers to actually complete post-market study commitments.

Finally, the Nov. 1-2 FDA hearing on drug advertising raised the issue of the explosion of Internet-type information about prescription drugs, and how many of these 'ads' fail to give appropriate weight to adverse events, or are otherwise unbalanced. This is a whole new world of potential abuse that the FDA needs resources to understand. Those hearings also included information about the growing level of device advertising that involves serious surgery and home testing kits that may or may not be safe. Clearly, more resources are needed to stay on top of these evolving media markets and products.

4. Resources to help bring lower cost, safe drugs and devices to market.

In addition to safety, a key consumer issue is the high price of drugs. We support efforts to bring, safe, lower-cost drugs to market as soon as possible. Additional resources could help reduce the backlog of generic drug applications. We also urge the FDA to begin to create now a system for the approval of safe "follow-on" biologics. Over the long-term, there may be no more important way to moderate pharmaceutical inflation. The scientific issues in this area must be made a priority now at the agency.

5. Resources to implement a conflict-of-interest free advisory committee process.

Obviously, the Congress expects the FDA to do a better job of finding advisory committee members without conflicts of interest. While this should be a minor additional expense, extra resources will be needed. This is just one more example where the FDA needs the resources to do a better job for the public interest.

6. Safety in the Institutional Review Board/Phase I trial process.

We have not independently investigated the issue of Institutional Review Boards (IRB) and the initial testing/Phase I process. But if the Bloomberg News reports[9] published in early November are even half correct, it is a scandal and a tragedy that threatens individual lives and the very quality of the drug testing process. The news reports indicate an almost total failure of the FDA to monitor this part of the drug development process. As the investigative news reports indicate, additional attention and resources should be given to this sector, with a performance goal of inspecting all private contractors by a date certain.

The Need to Help Consumers Choose the Most Effective, Safest Drugs

We believe that the government should require more scientific, evidence-based studies to help regulators, scientists, doctors, and the American public understand which drugs are truly effective and safe — and how drugs compare in effectiveness to each other, not just to placebos. And to slow the unsustainable growth in health costs, we need a comprehensive understanding of

[9] Bloomberg, "Drug Industry Human Testing Masks Death, Injury, Compliant FDA," November 2, 2005.

what is the best course of treatment across a variety of treatment options (for example, surgery, radiation, devices, medicines, life-style change, etc.).

The Medicare Modernization Act of 2003 provided the beginning of comprehensive comparative effectiveness studies in Section 1013, which authorized such sums as necessary for AHRQ-directed research. If this section were adequately funded to undertake a wide array of high quality clinical trials, the nation could save billions of dollars in the future by eliminating unnecessary and ineffective medical treatments and medicines. Unfortunately, the battle in Congress this year is over whether the amount appropriated should be $15 million or $20 million — a tiny drop in the bucket compared to what is needed. Given the long-range Federal fiscal situation discussed earlier, Section 1013's potential is likely to go unrealized, with a yearly fight for a small appropriation.

Therefore, we hope that PDUFA re-authorization will be accompanied by requirements for Phase IV trials that require new drugs be compared for effectiveness against other drugs in their class. PDUFA resources should be available to help FDA staff ensure that these studies are high quality and completed on time. A recent Health Affairs article proposed a 25% surcharge on the current user fees to fund a series of comparative randomized controlled trials on the safety of drugs used for the long-term treatment of chronic illnesses. While we would certainly support this type of proposal, we believe much more needs to be done. Requiring all follow-up safety trials to measure safety and effectiveness against other drugs in their class, and not just against placebos, would provide the extensive information that we need.[10] These studies, combined with the kind of data that should be available from the Medicare payment data base will finally begin to give us hard information on what works best — and least — in the world of health. FDA can and should lead in helping our nation slow the unacceptable rate of health inflation: understanding comparative effectiveness is the key to this struggle.

Consumer Reports Best Buy Drugs Campaign

Consumers Union is making its own effort in this area. We have combined drug pricing information with the data from the Drug Effectiveness Review Project (DERP) led by Oregon's Health and Science University to make recommendations to consumers on what is the Best Buy Drug. Our recommendations are saving individual consumers hundreds and thousands of dollars per year by encouraging: (a) people to take needed medicines, and (b) the prescription of effective and safe drugs that cost less than competitor drugs in a class.

The DERP project is being used by 14 states to assist in the development of their public program preferred drug lists (PDLs). This helps ensure that the most effective drugs are made available to Medicaid patients, state retirees, and others. A number of states have also shown how the use of these evidence-based PDLs can be used to save millions of dollars through competitive bidding procedures. To the extent the FDA can require good clinical comparative trials, you will help the

[10] See for example, Barton & Emanuel, "The Patents-Based Pharmaceutical Development Process: Rationale, Problems, and Potential Reforms," JAMA, October 26, 2005, p. 2081: "Rigorous comparative testing of drugs is highly desirable but should only be required postapproval. One option is to make FDA approval conditional on results of at least 1 randomized trial with a comparator in the same class."

DERP process and help the states improve the quality of their drug insurance programs, thus saving lives and dollars.

Conclusion

Thank you for your consideration of these recommendations that we believe will help improve the quality and safety of health care in the United States, and moderate the rate of health care inflation.