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Larry D. Sasich, Pharm.D., M.P.H, FASHP
Public Citizen's Health Research Group
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The FDA's Public Meeting on the Prescription Drug User Fee Act (PDUFA)

September 15, 2000

Public Citizen appreciates this opportunity to comment on the Prescription Drug User Fee Act (PDUFA) and what we hope will be its non re-authorization in September 2002.

When first put forth in 1992, PDUFA appeared to be a reasonable attempt to improve a drug review process reeling under chronic, imprudent under-funding of the Food and Drug Administration (FDA) by Congress. PDUFA's re-authorization in 1997 opened the door for passage of the Food and Drug Administration Modernization Act (FDAMA). This ill-advised law included such anti-consumer protection provisions as the off-label promotion of drugs and its dangerous pharmacy compounding provisions, neither of which remotely relate to the FDA's drug review process which is the subject of PDUFA. This highlights the dangers to the public of re-opening the Food, Drug and Cosmetic Act (the Act) every five-years giving the drug industry and its paid advocates in Congress the opportunity to play mischief with the Act. The toxic duo of PDUFA-FDAMA has weakened the FDA and for the first time rolled back consumer protection laws that had become progressively stronger during the last century.

By law, PDUFA fees can only be used for drug review. However, PDUFA-FDAMA mandated additional unfunded burdens upon the agency such as those mentioned above. Moreover, PDUFA-FDAMA requires that the amount the FDA must spend from public appropriations on the drug review process is increased by an inflation factor every year. With flat appropriations, funds for other vital FDA functions must be funneled into the new drug review process to meet PDUFA-FDAMA requirements for drug review funding. Consequently, resources for programs such as postmarketing safety surveillance, monitoring of prescription drug advertising, and manufacturer and import inspections, have dwindled.¹

PDUFA, via FDAMA, also resulted in a legislated "mission" for the agency² that has in effect recast the FDA as industry's partner, rather than its monitor, in new drug development with the intent to speed up the entire process – a role that economically benefits the industry. This new Industry-FDA culture of collegiality is not necessarily in the interests of the public's health.

During Public Citizen's 29 years of observing the FDA, the essential policy issues have remained largely unchanged. Primary among these is the relationship

In contrast, the effect of PDUFA on the last two categories of drugs is very troubling. Public Citizen is as concerned about what we perceive as a pressure to approve new drugs that would not have been approved before PDUFA, by lowering drug approval standards, as it is about the speed at which drugs are now being cleared for marketing since the advent of user fees.

Our survey of the attitudes of FDA Medical Officers completed in December 1998 revealed disturbing opinions about both the pressure and speed to approve new drugs. Thirty-four Medical Officers stated that the pressure on them to approve new drugs was "somewhat greater" or "much greater" compared to the period prior to 1995.⁵

Three recent examples from category 3, where there was an apparent pressure to approve, are the heart drug Posicor⁶, Duract⁷, an anti-inflammatory painkiller, and the antibiotic Raxar⁸. These drugs were approved between June and November 1997, just prior to the re-authorization of PDUFA. All had known safety problems prior to approval. All were redundant and there were multiple options available to patients and physicians for the indications for which these drugs were approved. All received standard reviews, and all killed and injured before they were withdrawn from the market between June 1998 and October 1999. We do not believe that these drugs would have been approved in the pre-user fee era.

With respect to the speed of drug approval, priority reviews are now being inappropriately granted for new drugs with, at best, modest effectiveness simply because they work by a new mechanism of action. Recent examples of drugs in category 4 are the type-2 diabetes agent Rezulin⁹, the flu drug Relenza¹⁰, and Lotronex¹¹, approved for the treatment of irritable bowel syndrome in women with diarrhea as the main symptom. Rezulin has been banned and the other two drugs have required significant changes to their safety labeling. Twelve Medical Officers in our survey identified 25 new drugs that they reviewed in the past three years that in their opinion had been approved too fast.⁵ The recent experiences with these drugs suggest that priority reviews are being abused and that drugs with new mechanisms of action raise the possibility of new mechanisms of toxicity.

2. Should the FDA continue to have performance goals for the drug and biological review process?

PDUFA-FDAMA's performance goals are in fact legislated deadlines that leave the agency with little flexibility. Reviewing new drug research is not a "cookie-cutter" affair. It is a process that is too important to the health and safety of the public to be constrained by time lines dictated by industry and enforced by the possibility that these funds will be cut off. This places enormous pressure on FDA reviewers whose decisions may affect the safety of millions.

an injury or death was drug-induced? Might the FDA be required to allow the industry final editorial approval before any advisory statements about drug safety were released to the public? All are possible with user fees.

The solution is clear - to prevent further incursion into the FDA's ability to effectively regulate prescription drugs requires public funding of the FDA. PDUFA-FDAMA is an unmistakable warning that user fees collected to finance the review of new drugs are bad public policy and that this scheme for funding the FDA must be regarded as a failed experiment.

(Department of Health and Human Services. FDA Creates Medication Guide For Lotronex – Health Professional Labeling Revised to Help Manage Risks. August 24, 2000.)

Public Citizen's Health Research Group petitioned the FDA on August 31, 2000 to immediately ban Lotronex. As of August 28, 2000, it has been associated with at least 26 cases of ischemic colitis, a condition that results from a lack of blood flow to the colon, leading to death of bowel tissue. (www.citizen.org/hrg/PUBLICATIONS/1533.htm)

12. Thompson L. User fees for faster drug reviews – are they helping or hurting the public health? *FDA Consumer* September-October 2000.

13. Honig SF. FDA Medical Officer Supplemental New Drug Application for tamoxifen (Nolvadex). October 21, 1998.