Committee of Ten Thousand

Advocates for Persons with HIV / HCV

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Testimony at FDA Input Meeting Regarding PDUFA IV
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The Committee of Ten Thousand considers the Prescription Drug User Fee Act contrary to protection of the public health. It is bad policy introduced at a historical time when many Americans were clamoring for drugs to combat the growing AIDS epidemic. For those whose goal was the accelerated approval of AIDS drugs it provided a format for expedited approvals. For those whose goal was less FDA regulation and increased industry influence and control, however, it has been the perfect vehicle for compromising the very mission of the Food & Drug Administration.

With the adoption of PDUFA Congress became the agent for this destruction. No longer would FDA function as the watchdog of our citizens' safety. After passage of PDUFA they became the paid consultants of the pharmaceutical industry, the technocrats of fast-track.

At bottom, PDUFA turned control of the Food & Drug Administration's finances over to the Pharmaceutical industry. Dr Sidney Wolfe of Public Citizen has said it succinctly recently: "**The public is getting the kind of FDA that that the Industry is paying for them to get.**"

Allowing applicants to pay for "objective" reviews by an agency they can thus control is nothing short of corruption of the federal government's regulatory responsibility. But undoing PDUFA, and returning to an annual appropriation for FDA drug reviews, requires finding replacement dollars in the Fiscal Year budget. Using FDA's own estimate, this amount currently is just under $400 million. However, for the first time in many years, there is a wide range of public interest organizations who are working with specific congressional members and committees to return the FDA, its mission, and it's funding to a foundation in sound public policy.

The biggest unintended consequence of the change in the source of funding is the relative poverty into which other regularly appropriated FDA programs have comparatively sunk. This is why a MDUFA was passed several years ago to allow the Center for Devices and Radiological Health to boost its device applications review process. However, the worst damage is in the FDA programs in the Center for Drug Evaluation and Review itself, whose other programs have atrophied under the reign of PDUFA.

PDUFA ensured that Phase IV post-market surveillance studies stood no chance of being mandated or adequately funded. The FDA does not currently have the authority to require Phase IV post-market studies. They can ask and they frequently do ask; however, there exists no direct enforcement vehicle for ensuring compliance by drug manufacturers. The agency is wholly dependent on the science generated by those who stand to significantly profit from the approval of

a given drug, biologic, or device. Industry driven science has wholly replaced, good, independent FDA driven research rooted in the public health not the profits of large pharmaceuticals.

How can the agency tasked to regulate the pharmaceutical industry simultaneously be dependent on that very industry for its budget and the lion's share of its science? It is nothing less that a prescription for disaster. We in the hemophilia community, the canaries in the coalmine as the early warning system for this nation's blood supply, have already suffered through two nightmares, HCV and HIV. Both were, in part, driven by conflict of interest and the complete lack of post-market surveillance. For us, acceptable safety margins can only be attained in the context of a fiercely independent Food and Drug Administration; fully funded, generating its own science, and tracking drugs, biologics and devices already in the market pipeline.

VIOXX and Cox-2 inhibitors are just the latest example of both inadequate testing and non-existent post-market surveillance. Fast-track approval in the absence of post-market surveillance can only result in overall reductions in the safety margins of our nation's drugs, biologics and devices. What has historically been defined as the FDA "gold standard" of drug and biologic approval has been degraded by PDUFA and the general conflict-of-interest climate that dominates the Food & Drug Administration in 2007.

Twenty-five years after the outbreak of the AIDS/blood epidemic, 8000 persons with hemophilia dead, and we have not learned the lessons of how conflict of interest was a critical factor in that worst medical disaster in US history.

Our organization represents persons with hemophilia who were infected with AIDS and hepatitis C in the 1970s and 1980s when the United States' Blood Supply was contaminated with these viruses. Industry has paid $650 million dollars to our families in recognition of their failure to rapidly begin a standard program to screen potentially infected donors, and, their failure to use adequate available processes in the manufacture of blood products to eliminate such viruses.

FDA's lack of oversight in this period, when entire lots of factor concentrates suspected of being infected were nevertheless approved for sale, was unconscionable. Moreover, FDA allowed industry to deplete existing stocks of potentially infected product for sale and infusion by members of our families, before using newly processed product, free of infection. In recognition of these shortcomings by its regulatory agency, the federal government paid another $650 million to our families.

$1.3 Billion brought back none of our children. Our organization's name derives from estimates that our community was approximately 20,000 strong in 1980; approximately one-half contracted HIV. Even more contracted HCV. Few such individuals are still with us.

In bringing current these horrific events of a generation ago, a generation largely missing from our community, we underscore how serious the Committee of Ten Thousand, or COTT, is about drug oversight by the FDA.

In the 1980s and early 1990s, the AIDS community, of which we count ourselves as a member, was active in efforts to encourage FDA to create a fast track for AIDS drugs review. However, where COTT differed from the majority of groups calling for fast-track AIDS drugs was in our

call for **post-market surveillance as a critical component of any initiative to expedite the approval process**. Given the AIDS/blood epidemic, we in hemophilia intimately understood the need for serious tracking of approved drugs, especially drugs approved on a fast-track. Considering the years since the advent of the virus on our shores in the late 1980s, and the little that had been done in research or drug development at that time, there was a crying need for FDA-approved medications for a population that to this point merely had had a death sentence over its heads. However we certainly never supported fast-track becoming the new methodology for all drugs.

When AZT was found effective under Protocol 019, ending in 1988, the door began to open. Only six years later a combination of therapies was available that greatly increased the lifespan and quality of life for those afflicted with HIV/AIDS.

But FDA continued to use fast track, and recipients of many such approved medications were thankful and became natural protectors of the fast track process.

Unfortunately, in the same time period, with the influx of a new conservative majority in Congress, the idea of speeding drug reviews by requiring applicants to pay for the review was made a part of their platform, and in the name of the same fast review as the AIDS community had requested, it became law. Republican governments since that time have routinely re-authorized the process, which has, over 15 fiscal years, allowed the need for appropriated funds for FDA new drug review to atrophy completely.

The FDA still relies on voluntary submissions to its Adverse Event Reporting System; informing the medical profession that to minimize the inconvenience of reporting, only death defines "Adverse Event." Seven different drugs, including Duract, Posicor, Rezulin, Baycol and others, have been recalled after approval since 1996. Others may be in current use, with harmful effects going unreported and no FDA response triggered. It is a soft surveillance system at best.

The FDA still relies on promises. When a drug is approved, the developer is told of the conditions for approval, for example manufacturing parameters, as well as dosing limitations. When trial data or other information suggests the potential for harmful effects not seen in the required pre-approval clinical trials, the developer is ASKED to do post-market surveillance studies. If it does not agree, approval is denied, so of course all agree, or promise, to spend the additional funds to conduct a large-scale, carefully designed "Phase IV" trial, with a large enough "N" and a long enough duration to identify any less-prevalent harmful effects. FDA reports annually on how many of these promised studies have been even started. The average is one-third or less.

Where is the enforcement? Is it in FDA's recalling the drug once in wide distribution? Unthinkable. But without <u>some</u> enforcement power, and a revived agency to carry it out, drug developers scoff at promises they give regarding safety, and at FDA itself.

The current situation is a circus. Only in recent years have efforts begun in Congress as well as FDA to restructure the agency to get back to its job of regulating. For our part, we oppose PDUFA and will work to see that these proposals include terminating it and finding dollars to put new drug approval back into the FDA's annual appropriations.