Statement of Kim Witczak
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on behalf of

Woodymatters

before the
Senate Committee on Health, Education, Labor, and Pensions hearing

on
Drug User Fees: Enhancing Patient Access and Drug Safety
March 14, 2007

Mr. Chairman, Senator Enzi, Members of the Committee:

Thank you for inviting me to testify today.

I am here today to represent the voice of thousands of families who live every day with the consequences of the current drug safety system. Unfortunately, I know first hand what it feels like to lose someone because of unsafe drugs. On August 6th, 2003, my life changed forever. I became a widow.

My husband of almost 10 years was found dead hanging from the rafters of our garage of Zoloft-induced suicide at age 37. Tim Witczak, known to most as Woody, was not depressed nor did he have a history of depression or any other so-called mental illness. Woody had just started his dream job as Vice President of Sales with a start up energy efficient lighting company a couple months prior and was having difficulty sleeping which is not uncommon for new entrepreneurs. So Woody went to see his general physician and was given Zoloft for an insomnia diagnosis. Five weeks later, Woody took his own life. His doctor gave him a 3-week Pfizer-supplied sample pack that automatically doubled the dose after week one. No cautionary warning was given to him

or me about the need to be closely monitored when first going on drug or dosage changes. In fact, I was out of the country on business for the first 3 weeks he was on Zoloft. When I returned, I found Woody one night in fetal position on our kitchen floor with his hands wrapped around his head like a vise, crying, "Help me, help me. I don't know what is happening to me. I am losing my mind. It's like my head is outside my body looking in."

Never once did we question the drug. Why would we? It was FDA approved, heavily advertised as safe and effective, AND it was given by Woody's doctor that he has seen for years and trusted.

From the beginning, something didn't add up about Woody's death. So my brother-in-law, Eric Swan and I started researching the only thing that made Woody change during this extremely short period of time. Zoloft.

In our battle for Woody, we were able to get confidential internal drug company and FDA documents made public that showed the side effect that killed my husband and many others was known in the original clinical trials from the 1980s. In fact, according to a 1990 internal FDA memo, Dr. David Graham expressed concern that he didn't think Eli Lilly adequately addressed the suicide risk with Prozac. In 1991, the FDA held a public hearing on the antidepressant induced suicidality in adults taking Prozac. At that time, the FDA determined that further studies were needed to look at suicidality. The drug companies did not conduct studies even though protocols were created. Subsequently in the years to follow, more antidepressants entered the market with millions of adults and now children taking the drugs. With mounting pressure and other countries reporting the link between antidepressants and suicide, the FDA held another public hearing in 2004 on children and antidepressant induced suicidality. It ultimately led to a blackbox warning for children under 18 and the FDA agreed to review clinical trials to see if the risk exists for adults. In December 2006, 15 years after the first public hearing, the FDA held another hearing to share their findings on link between antidepressants and suicide in adults. [It is interesting to note that it's literally the same people conducting the review and approved the drugs in the first place.] After reviewing the original clinical trial data, the FDA recommended that the blackbox warning further be extended to adults 25 and under. The FDA acknowledges that the suicide risk exists in people taking antidepressants – adults and children. Why would you confuse the public by not warning ALL people of the suicide risk? If my husband were still alive, the current FDA recommended blackbox warning would not cover him because he was 37 years old.

Our journey for the truth has led us to the FDA, HHS, Congress and the Courts. In fact, this is our 25th trip out here since Woody died. Unfortunately, Woody's story is not an isolated case (or anecdotal story). I have been working with many other families who have lost loved ones due to unsafe drugs and they could tell similar stories. Woodymatters was founded to give a voice to Woody and our activism. The website also gives other families a chance to tell their stories and get information.

I tell Woody's story in the hope that you will use the once-in-five year opportunity of PDUFA extension to make fundamental reforms in FDA, so that other families will not have to suffer what I and so many others have endured.

To be blunt, the draft agreement reached between the industry and the FDA is totally inadequate.

First, let me say for the record that consumers, most legitimate patient groups, and the Institute of Medicine are deeply troubled by the whole user fee program. The FDA is one of America's most vital public agencies, and its duty is to ensure the quality and safety of over a fifth of our economy. Its client is the American public, and therefore it ought to be funded totally out of the general Treasury. If user fees are needed in lieu of general appropriations, then there should be no conditions attached on how that money is spent. I support legislation that Rep. Maurice Hinchey proposed in the last Congress, which breaks the morale-destroying conditions that are part of the current PDUFA system.

If breaking those ties is not possible, then we need increased resources for safety and the post-approval drug monitoring process—and we need specific goals for the use of those resources, just like industry gets on the pre-approval side.

The Institute of Medicine report did not give one specific number for the cost of its various recommendations, but it appears to be between $100 million and $200 million. The draft industry-FDA agreement provides for only about $29 million for increased safety. Some of that $29 million is said to be earmarked (we'd like to see the specific language of how that will be done) for some very worthy improvements. For example,

> --the proposal would no longer limit how long user fees could be spent on a specific drug's post-market approval safety issues (it eliminates the current two to three year limit), since, as the FDA says, 'current data show that safety issues can arise after a drug has been on the market for 8 or more years;
>
> --PDUFA IV monies could be used to 'obtain access to additional databases and increase program staffing with epidemiologists, safety evaluators, and programmers who can use these new resources.'

But all too much of the new 'safety money' is spent on 'let's just do more of what we are doing,' let's hold forums and symposia, let's develop 'papers.' For pre-approval, industry gets specific, rapid deliverables. In post-approval safety, we get placebos. That's a strong statement, but look at the draft agreement: The industry gets 90 percent of new drug applications decided within a certain number of days, and requests for meetings answered within two weeks. What does the consumer public get? We get sentences like

> "…FDA would use these funds to continue to enhance and improve communication and coordination between pre- and postmarket review staff."

We get phrases like:

> "Potential activities in this area might include integration of certain proposed recommendations made by the [IOM]."

And

> "a public workshop to identify best practices in this emerging field, ultimately developing a document that addresses epidemiology best practices…"

I urge you to amend the PDUFA agreement and/or section 107 of S. 484, to spell out additional resources for specific safety achievements such as:

--give the FDA the computer resources to detect dangers faster. S. 484 calls for the FDA to submit a strategic plan for information technology within a year. The FDA has told consumers that they need $20 million a year to implement their modernization plan, and that at the end of 2006 vendors would no longer serve over half their IT equipment because it is so outmoded. But I urge this Committee to require regular progress reports from the FDA on how they are using this money. I just had an opportunity to see the heavily censored "Breckenridge Institute" analysis of the FDA's efforts to modernize the Adverse Event Reporting System. The report describes incompetence and waste that is breath-taking. It describes a culture that explains how **antidepressants** and so many other drugs have been on the market for so long with so little **safety** action **taken**. As the Breckenridge analysts say,

> "one of the root causes of the confusion and delay surrounding the AERS II system from 2003 onward is a lack of effective leadership and management on the part of CDER's Office of Information Technology …CDER's culture can be characterized as one in which managers at all organizational levels fail to move from the awareness of organizational problems, to the kind of action that will produce positive change.

Please, I urge this Committee—*the Board of Directors of the FDA*--to make sure that the agency starts to move to action, and stops wasting precious time and money.

--within the next 5 years make sure the FDA's computers can use the goldmine of information available from Medicare part A, B and D data to detect what is dangerous and what works;

--do more to ensure the timely pre-clearance not just of TV ads, but of all advertisements and informationals, including ads on the Internet and at continuing medical education displays. My career is in advertising, and I can tell you that a goal of 30 to 45 days for pre-clearance of TV ads is much too long and will not

work for industry. I oppose direct-to-consumer advertising of drugs, but if you are going to do it, do it right, and that means doing it in a timely manner;

--the lying and falsification of data in the Ketek case is outrageous and you hear rumors of similar trial distortions (why is it that so many trials, especially Phase 4 post approval trials come in favorable to the people paying for the trial?). Spend PDUFA safety money to double the number of trials and investigational review board applications audited to ensure the ethical treatment of enrollees, and the integrity of the data;

--investigate all serious adverse event reports within 15 days; also program FDA computers so they can better detect patterns or clusters of adverse event reports to determine if REMS action should be taken. Clusters of AERs should trigger studies and trials to determine if there is fire where there is so much smoke;

--spend some money to actively recruit non-conflicted advisory committee members. As others have said, with about 125 medical schools in this nation, we ought to be able to develop a 'library' of experts who are conflict free and willing to serve. Without spending some money to recruit these people, it is too easy for the FDA to complain that they do not exist. As we can find more conflict-free experts, you can amend Title IV of S. 484 to require a gradually rising percentage of conflict-free advisors.

--spend money to take action (which may include the levying and collection of civil monetary penalties provided by S. 484) against at least 50 percent of the applicants who have failed to complete follow-up safety studies or trials. When the FDA was first reviewing anti-depressants in 1991, it ordered follow-up safety studies that were never done—and are part of the tragedy of Woody's story.

As I indicated above, I oppose direct to consumer advertising of drugs, because there are so many side effects and dangerous consequences that we do not know about until a drug has been on the market for years and even decades. To encourage overuse and the medicalization of every problem leads to the death and injury of many who may not really have needed a particular drug. Vioxx is a prime example. <u>If there is advertising, then the law should require that each ad include a 1-800-number where consumers are advised to report adverse side effects.</u> Currently, it is very difficult for consumers to use the FDA website to search for dangers in drugs. The whole website needs to be redesigned to be made easier for the public—starting with the use of the commonly advertised name of drugs. The public does not know the nearly unpronounceable, multi-syllable chemical name of drugs; the simple step of using the advertised name would be a huge improvement.

One other key point: there is nothing in PDUFA or that I can see in S. 484 that addresses the key FDA problem: the internal culture to "approve drugs quickly/consider safety slowly."

We all want life-saving drugs approved quickly, but the FDA is out-of-balance and must give more attention to post-approval safety.

You can legislate culture and staff morale, by improving the transparency of the agency and of the approval process.

First, I urge you to strengthen S. 484's Title III: report the results of all trials, within a year of the last trial on the specific drug, whether it is submitted for approval or not. In addition, trials of drugs that are currently on the market should gradually be included so that there is a public library of the scientific trials conducted in the last decade or so.

Dr. Steven Nissen, President of the American College of Cardiology testified before this Committee on November 16, 2006:

> When drugs show serious toxicity in patients, the results are rarely published. Accordingly, other companies subsequently expose patients to closely-related drugs without knowing that their competitors' study of a similar agent showed significant harm. I am aware of a class of drugs where more than a dozen compounds showed serious toxicity, resulting in termination of development, but without a single publication of results [emphasis added]. In my view, when a patient volunteers to participate in a drug or device study, there is an implicit moral obligation that the patient's participation will benefit medical science. When studies are not published, we learn nothing from the experiment and make the same mistakes over and over again.

In other words, fellow citizens have twelve times been subject to danger as human guinea pigs on a chemical or biologic that was dangerous, had toxic effects, and was a scientific dead end. That is outrageous. If Phase 1 results were made public, then after the first failure, eleven other sets of volunteers—probably over two hundred people--would not have been endangered, and the cause of science would have been advanced.

Publishing Phase 1 results can also speed drug discovery at lower cost. I find it ironic—and sad—that the pharmaceutical industry complains about the high cost of research, yet the results of unsuccessful trials that waste millions and endanger volunteers are hidden. The FDA's PDUFA discussion published in the Federal Register of January 16, 2007 says

> "Our experience and insight, gained through years of review, can help the industry avoid wasting scarce research and development resources on clinical trials that are not likely to produce results because of flawed designs.

True! And imagine how much more would be saved if the world scientific community could see the results of Phase 1 trials. If there is a proprietary secret, the patents surrounding the whole drug process provide some protection. But it is immoral to continue human guinea-piggism in the name of proprietary secrets and without advancing the cause of science.

If you have questions about making Phase 1 results public, I urge you to at least amend S. 484's GAO study about whether to report late Phase 2 trial results, and instead make it a study of whether to report Phase 1 results.

I obviously hope you will amend S. 484 to report all Phase 2 trials. That should be a given in the name of science and to facilitate meta-analysis studies of safety and effectiveness.

S. 484 provides for publication of a trial result two years after the final completion of the trial. I understand that this is to allow time for publication in peer reviewed medical journals. But I also understand that the world of medical journal reporting is changing rapidly to be quicker and more electronic, and that some are urging that the great journals concentrate on discussions of the implications of findings from one or more trials, and not be a slow, front-line source of basic trial data. Certainly in cases where the trial or study has raised concerns about aspects of a drug on the market, a way should be found to make that data public for further study by the world scientific community.

Mr. Chairman, Senator Enzi, I particularly appreciate the provision in S. 484 that requires both a technical and a more-laypersons descriptions of the results of clinical trials. A relatively 'user friendly' version will empower patients and patient advocates to understand better the drugs that are available and whether they want to 'dig into' the more technical explanation.

There is a second major transparency step that Congress should legislate: make the details of all FDA approval decisions public within a month or two of approval, so the world can see what the issues are and what needs more study. By legislating disclosure you can instill a climate of scientific openness and dissent so the staff's morale is restored. Those who say that having pro and con data public about a drug will confuse the public and cause drugs not to be used are just saying that we consumers and—even worse--our family physicians are too dumb to understand or too stupid to handle complexity. They obviously have never lost a loved one to a drug reaction. It is an arrogant argument, and it is an insensitive argument—and it certainly doesn't fit with all the talk I hear from Washington about patient empowerment and 'shopping' for health care.

I would like to see a separate and independent Office of Drug Safety, as Senator Dodd and Grassley have proposed. It is telling that the current office is called Surveillance and Epidemiology—not exactly a clear message to the general public! The public needs to hear a clear message about this office—a message like you see on construction sites: Safety First! The Commissioner and many others oppose such a separate office, saying it would be a duplicate bureaucracy and slow up approvals.

I'd like to offer a solution: Give the head of Drug Safety (currently the head of the Office of Surveillance and Epidemiology) the authority—and the responsibility—to say he believes there are enough safety questions about a drug, pre- or post-approval, that the

drug should not be approved, or if approved, that REMS (as established by S. 484) should be adjusted, or that it should be pulled from the market. If the head of the Office of New Drugs disagrees, the two Office heads present their cases to the Commissioner within a date certain, say a week, and he makes a decision within a day. This would not slow down the process, but it would make a career professional physician-scientist responsible for standing up for safety when he thinks the facts justify it. Today, there appears to be little or no accountability for the woeful saga of Ketek and other questionable drugs. This process should, of course, be very public, with reports to Congress on the details of when such disagreements have arisen and how they were resolved. In addition, points of contention should be subject to Advisory Committee review and comment by national and international experts.

Under my idea, there would be no separate bureaucracy. No new expense. The two offices would still work together. But there would be accountability. Doesn't that bridge the argument pro and con a separate Office of Drug Safety?

There is a great deal more I could say. But in conclusion, I think transparency and openness is the key to restoring the FDA as the world's 'gold standard' in drug approvals and safety. Dr. David Ross, currently with the NIH, recently left the FDA with, I gather, a great deal of sadness and frustration. He has described the FDA decision-model as very military and one that squelches dissent. Once a decision is made, no more questions! And as he says, that can be necessary on a battlefield. But the FDA is a scientific organization, and the heart of any such organization is open-mindedness, willingness to look at new data, and flexibility. If the culture of the FDA became one of openness, there would be fewer future drug disasters, and I gather it would be a much better place for scientists to work.

Mr. Chairman, Senators, it is said the history of the FDA is written in the tombstones of drug and food safety disasters.

Stop the march of tombstones.

Do what is right for the American public.

Give us a strong, well-funded FDA.