

FDA's Drug Approval Process: Up to the Challenge?

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President

Testimony

Mr. Chairman, members of the Committee, thank you for inviting me to testify today about the Food and Drug Administration's (FDA) approval process, drug safety and the concerns of patients. I would like to offer possible solutions to the growing controversy about the safety of medical products that are regulated by the FDA.

The National Organization for Rare Disorders (NORD) is a non-profit voluntary health agency dedicated to the identification, treatment and cure of rare diseases through programs of education, research, advocacy and services to patients and families. Because most patients with rare diseases have no or few treatment options, our primary goal is to encourage research and development of new "orphan" drugs and biologics and "humanitarian use devices" (HUD).

We are grateful to Congress, through the Orphan Drug Act and annual appropriations, for its support of those living with rare diseases. Today, there are 266 FDA-approved orphan drugs on the US market; and the National Institutes of Health (NIH) and the FDA are doing more to help us each year. However, there are more than 6,000 known rare diseases, so there is still much to be done.

The FDA is the nation's watchdog for pharmaceuticals, biologics, medical devices, veterinary medicines, foods and cosmetics. These products account for about one-quarter of every dollar the American consumer spends each year. Yet, the FDA is given meager federal resources to ensure that these products are safe and effective.

Recent health crises arising from FDA regulated products threaten to weaken the public's trust in the Agency. Some of these drug safety issues include:

- Cox-2 inhibitors, used to ease the pain of arthritis, have been found to cause increased rates of heart attack and stroke;
- Most antidepressants have inadequate proof of safety and efficacy in children, but they are commonly prescribed for this population even though most are not approved for use in children;
- The influenza vaccine shortage can be traced to a factory in great Britain that failed FDA inspection;
- Estrogen, taken by millions of women, has been found to cause increased rates of heart attacks and stroke; and,
- In late February, the FDA issued a warning that two new drugs for psoriasis, which are being widely used off-label on a chronic basis, have been associated with cancer and

serious autoimmune diseases.

These problems follow other drug withdrawals in recent years that killed or endangered our citizens, such as Fen-Phen diet pills, the cholesterol drug Baycol®, and the diabetes drug Rezulin®.

The public is now asking some important questions. Could the FDA review process have discovered or anticipated these problems before the products were marketed? Once these drugs were on the market, could the FDA have acted to protect the public sooner in any of these or similar cases?

A key source of misjudgments by the FDA is a relative imbalance in the time allotted to review drugs for serious- and life-threatening diseases versus less vital pharmaceuticals. This has been aggravated by the user fee system and is complicated by the two different patient constituencies that the agency serves.

First, most of the public are generally healthy and require medicines for temporary and benign illnesses such as the common cold. They usually do not want to be exposed to risks. They want the FDA to ensure their treatments will be near to absolutely safe and reasonably effective.

The second segment of FDA's constituency is people with serious or chronic diseases such as rare diseases and cancer. These individuals want new treatments as quickly as possible and are often willing to bear substantial risks in exchange for possible efficacy. For example, cancer drugs are often known to be very toxic, but a person who may lose his or her life to cancer is usually willing to take highly toxic chemotherapy drugs and suffer horrendous side effects in exchange for a hope of recovery.

These disparate groups bring tremendous political pressure to bear on the Agency. On the one hand, the FDA is pressured to approve drugs quickly for very sick people, when the drugs have minimal scientific evidence. On the other hand, the Agency is compelled to review drugs with more deliberation to avoid risks for healthy people.

Unfortunately, most consumers do not know enough or have sufficient skill to perform sophisticated risk/benefit analyses applicable to their own situation. What appears on the official FDA approved "labeling" for a drug is rarely helpful. It is written in medical terminology and printed in tiny fonts. It is very difficult for patients to get accurate information that is readable and understandable without medical training.

Instead, on a day-to-day, drug-by-drug basis, patients must rely on their physicians to interpret whether a particular product is safe and efficacious for their particular circumstance. And both patients and physicians must rely on the FDA to weigh risks versus benefits, and to ensure that the marketed drugs are not unsafe or ineffective.

Another tension arises from the way that clinical trials are constructed in order to comply with the scientific method. In a perfect world, a clinical trial would be one in which all patients were completely identical in every regard, except who received the study drug

and who got placebo. The double-blind, placebo controlled study does, in fact, bring us closest to knowing whether a drug is safe and effective. What we often do not learn from clinical trials is the safety and effectiveness of a medicine when used in the wider heterogeneous population for which it will ultimately be prescribed. Clinical trials are never true mirrors of the real world.

Once a drug comes to market, people who take other medicines and have other diagnoses will take the drug and they may suffer an unanticipated adverse reaction. This means that labeling changes are often needed after a drug reaches the market, but the FDA does not “tell” companies to add changes to their labels. They “negotiate” the changes with manufacturers. Meanwhile, more patients may suffer adverse events because doctors are unaware of the problems associated with that particular drug.

The FDA must be given the authority to require manufacturers to do things that will enhance patient safety without delay, and they especially need the authority to impose penalties if companies do not comply.

We see many other areas of concern, some of which represent serious problems. Congress should examine and then rectify these items:

FDA Commissioner

The FDA has had a Commissioner for only 18 months out of the past four years. This also means many of the top managerial positions at the FDA are vacant. This sends a sad and dangerous message that the public health is not a high priority to our government. Without a Presidentially-appointed, Senate-confirmed FDA Commissioner, no one knows where the buck stops.

Appropriations

I have been dealing with the FDA for over 25 years and no matter who is in the majority, funding for the Agency has never been a high priority to Congress. A major problem is that the Agency is not funded through any of the health-related appropriations committees. Rather, it is funded, for historical reasons, by the agriculture appropriations committees. There, FDA’s funding must compete against fish farms, diseases of peach trees, and the tobacco subsidy. One father told me that the government spends more money researching the diseases of shrimp than the rare disease that is killing his two sons.

Furthermore, when Congress so generously doubled the NIH budget, no one seems to realize that the ultimate success of NIH research is the development of more treatments and cures (NIH Roadmap). So for every dollar Congress appropriated to the NIH, they should have increased the budget of the FDA. Instead, the FDA has suffered from meager funding increases and a higher reliance on user fees.

Measures of Success

Under the Prescription Drug User Fee Act (PDUFA), the FDA's performance is measured by its speed in reviewing new drugs, not on the scientific quality of its reviews. The Agency is not allowed to spend user fee revenues on anything other than new drug reviews, so it does not have enough funding for post-marketing surveillance of marketed drugs, nor to monitor pharmaceutical advertising.

Enforcement Authority

The FDA does not have adequate enforcement authority, and it cannot set reasonable penalties if companies violate regulations. For example, the FDA sometimes requires companies to conduct Phase 4 studies after a drug is on the market, the statutory penalty for non-compliance being the removal of a drug from the market. This would punish patients as much or more than it would a company. So the FDA continues to require Phase 4 studies, and the companies continue to ignore the Agency's directives.

Direct-to-Consumer Advertising (DTCA)

If the FDA sees a misleading television ad about a drug, it can require the ad to be pulled off the air. Unfortunately, the rules regulating DTCA for prescription drugs allow companies to print or broadcast their advertisements before the FDA review and approve them. So the harm is already done and millions of people have been influenced by the misleading ad before it is pulled off the air. The Agency needs adequate staff to monitor and review advertising BEFORE it is broadcast or printed.

We suggest that companies might be given a "safe harbor" if the FDA approves their advertisement before it is disseminated. Otherwise, they should suffer high civil monetary penalties if they circulate an ad that is misleading or inaccurate without FDA's pre-approval.

Safety Monitoring and Surveillance

In response to sharp criticism, the FDA recently announced the creation of an "independent" drug safety monitoring board made up of government employees. Rather, we believe it should be composed of medical and scientific experts from outside the federal government, and it should report directly to the Commissioner's Office, with FDA employees serving in an advisory capacity only. Consumers should also be well represented. Again, if the perception among consumers is that the Agency is beholden only to industry, it stands to reason that any decision coming out of this new safety monitoring board – composed of government employees only – would be considered suspect.

The post-marketing surveillance system currently in use is seriously flawed and needs to be reworked at every stage of the process. The current system relies on voluntary adverse

event reports from doctors and hospitals, but it is generally agreed that only a fraction of the AE reports are ever reported. Again, the FDA has been mandated by Congress to monitor the AE database to detect any serious patterns, but funds were never appropriated for that purpose.

Given the authority to extract monetary penalties from industry when there are egregious violations of the law, the FDA could use those funds for post-marketing surveillance safety studies as well as DTCA monitoring.

Priority Reviews

Since user fees were instituted at the FDA, the Agency has placed undue emphasis on drugs that are not medically important. Beginning in the 1980s, through the first half of the 90s, priority reviews were given only to treatments for serious and life-threatening diseases (applications were reviewed within six months, and sometimes faster). Standard reviews, averaging one year, were given to all other drugs.

Many consumer groups believe that expedited approvals should be reserved solely for serious- and life-threatening diseases. Drugs for non-life-threatening diseases and disorders should not be given fast reviews when there are many alternative treatment options available. As I mentioned earlier, the majority of consumers do not want to be exposed to serious risks in exchange for a temporary symptomatic benefit.

Transparency

The FDA is probably one of the most secretive government agencies that any consumer will ever have to deal with. Virtually everything about a drug is considered proprietary. Consequently, Agency officials will not talk with anyone about the drug unless the manufacturer gives them permission to do so. Today, consumers are demanding greater transparency. This is our government and the FDA is here for us. We should not have to write Freedom of Information letters to find out why there is a shortage of a medicine, or how many other people taking a specific medicine have suffered an adverse event. Doctors and patients need answers. The FDA's secrecy is inexcusable.

The industry counters with the argument that "trade secrets" can not be disclosed, but because of this insistence on secrecy, consumers become increasingly suspect that important facts that could affect their health are being purposely hidden. Why were the studies showing that antidepressants were safe for children published, while other studies of the same drugs showing that some children died, kept secret?

There is the perception among many consumers that the FDA is beholden only to the industry. True or not, the FDA decision-makers should be reminded that their decisions affect lives. They should be reminded that they are not the Defense Department with national security concerns. They should feel free to answer the concerns of consumers readily and factually.

Summary

The FDA is a critically important public health agency that regulates products consumed or used by every person in this country. Consequently, the Agency must be high on the list of Congressional priorities. Public health catastrophes would be less likely to occur if the Agency were substantially strengthened and had the full support of key Congressional Committees.

The FDA needs greater enforcement capabilities, and a substantial increase in funding to allow it to respond to public health emergencies. Its performance should be measured not on speed, but scientific evidence and excellence.

If Congress gives the FDA the tools, the Agency will secure the public's trust. For all the talk about less government and smaller government, the FDA is one area of government that the public wants more of, not less. People want assurances that the food on their table will not make them sick. They want to be confident that the medicines they take will enhance, not destroy, their health.

It is up to Congress to reinforce America's trust in the FDA, which guards our nation from medical catastrophes. It is Congress' responsibility to work with ALL stakeholders to strike a balance between increased innovation and safety and efficacy.

Thank you.

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