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Fixing the Broken Drug Evaluation Process at the FDA: 10 Initial Ideas

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When it comes to reviewing drugs, the FDA's job seems straightforward: Make sure a drug is safe. Then make sure that it actually works and does what it is supposed to. It's an essential mission that this deeply dysfunctional organization appears to be having trouble fulfilling. The EpiPen pricing scandal and the controversial approvals of flibanserin (Addyi) to improve underactive sexual desire in women and eteplirsen (Exondys 51) for treating Duchenne muscular dystrophy illustrate that the FDA appears to be having trouble following its own guidelines.

I have been working in investigational drug development for almost two decades. As a politically conservative medical scientist at the FDA - a supreme rarity, I assure you - who has worked as a medical officer and senior medical analyst at the FDA, and as a former investigational medicine research scientist at Pfizer, I haven't always agreed with regulatory decisions made by the FDA.

Lately though, in addition to disagreeing, I now fail to understand several of the FDA's decisions in the very recent past. In addition to a profound lack of scientific proof, these decisions seem to lack basic common sense. For example, flibanserin worked in only 8 percent to 13 percent of the women in which it was tested. On top of this pathetically poor efficacy, flibanserin can have life-threatening interactions with recreational alcohol consumption and some of the most commonly prescribed antibiotics and antifungals on the market.

Eteplirsen's recent approval by the FDA was deeply disquieting and like flibanserin, also sets a terrible precedent. Eteplirsen was tested in a mere 12 individuals, with no control group - a highly unusual situation when it comes to evaluating an investigational medicine. In addition, the drug increased production of a key dystrophin biomarker protein needed for improvement by less than 1 percent of normal overall, which is neither clinically nor scientifically meaningful.

As a former FDA medical officer and erstwhile FDA observer, I offer 10 of my many suggestions for fixing the agency.

Bring truth to prescription drug labeling. Many generic drugs are imported from so-called "sweatshop" countries such as India, China, Mexico, and Taiwan. These countries have very serious problems with falsifying records, unclean manufacturing environments, and poor quality control. Most people are pleased to give Walgreens or CVS $4 for a month's supply of their prescriptions and think they got a pretty good deal. But would they be just as happy if they knew these drugs were of poor quality and from sweatshop countries where egregious violations of the drug manufacturing process are commonplace? All consumer prescriptions should be labeled with the country of origin,

and patients should have the option to request that their prescription drugs are made in the US or a non-sweatshop country such as Japan, Germany, France, or Israel.

Fix the broken hiring process. The FDA's inability to hire enough qualified staff members has been an unaddressed problem for well over a decade. This hampers its ability to carry out its mission. Take, for example, the approval of money-saving generic drugs. The FDA has a backlog of as many as 4,000 applications to produce such drugs because it doesn't have the staff to review them. Part of the problem is a broken hiring system through USAjobs.com, where all applications must initially be submitted. There, human resources managers with little or no scientific training review the applications of highly specialized scientists. To make matters worse, it's impossible for the best and brightest in academia and industry to directly call a recruiter at the FDA, because there is no publically available list of FDA recruiters.

Negotiate disagreements between reviewers and management. Reviewers are responsible for conducting the hands-on component of drug analyses. They summarize what sometimes amounts to tens of thousands pages of data for others at the FDA, including management. If management (which did not conduct the review) disagrees with the in-the-trenches reviewer, that reviewer currently has no recourse except to obey his or her supervisor. Reviewers should have the option to contact an outside group of scientists - possibly a congressionally appointed committee. And the facts of such disagreements (which occurred with both flibanserin and eteplirsen) should be made public.

Have a role in drug pricing. The FDA currently has no say when it comes to the actual price of drugs. Congress should create an offshoot of the FDA similar to the United Kingdom's National Institute for Health and Care Excellence. It independently reviews and recommends drugs within the same class, based on their safety, efficacy, and overall merit and benefit. This is something we could definitely learn from the FDA's European counterpart, the European Medicines Agency.

Stop abusing startups and small drug companies. Like it or not, the US depends on private drug companies to invent and develop new drugs for existing and emerging diseases. I have personally attended numerous FDA meetings during which typically smaller drug companies that needed help developing drugs were verbally abused and demeaned by FDA staffers. FDA employees who are hostile towards private pharmaceutical companies trying to help the world through legitimate development of new medicines should be held accountable for such abusive behavior. Some sort of public rating system should be created that will let drug companies publically evaluate the helpfulness of FDA employees.

Improve workforce quality - consequences for bad decisions. Most FDA staffers and supervisors are highly qualified, dedicated individuals from dozens of different disciplines. That said, the FDA would benefit from a good personnel sweep. The agency has its share of petty people who have personal agendas against fellow FDA employees and/or pharmaceutical companies. Firing FDA employees who have attained federal "career" or "permanent" status - which amounts to university tenure - is difficult. They essentially have to be caught red-handed breaking the law in order to be fired.

Some FDA staffers in powerful positions make bad decisions, or have views which aren't in line with mainstream, evidence-based science. Directors, deputy directors, or others should be held directly accountable when they incorrectly approve a drug, unnecessarily hold up approval of one, or implement bad decisions, just as would happen in private sector jobs. Unfortunately, most of what happens in internal FDA meetings is never made public, so it is often difficult or impossible to hold individual accountable.

Improve the quality of advisory committees. The FDA often solicits advice from independent advisory committees on how to proceed when clinical questions arise. To be part of an FDA advisory committee, however, an individual must not have accepted any research funding or speaker's fees from a drug company or have any conflicts with the drugs being reviewed. Because the best and the brightest scientists are usually doing original or novel research, often funded by industry, this eliminates many of the most qualified individuals. As a result, today's advisory committees are usually made up of retired physicians and scientists who aren't leaders in their fields, and

aren't always up to date on the latest clinical developments. Advisory committee members need to be a lot better than they are, which will make their opinions hold more weight.

Address dangers of "right to try" legislation. As a politically conservative medical scientist, I am all for fewer laws and less government intervention. That said, I am not ready to entrust the average person to make informed decisions regarding investigational medicine, pharmacogenetics, and long-term safety of new, unapproved drugs. Those sorts of analyses are the entire reason we have the FDA in the first place. Americans disheartened with long FDA reviews, lengthy approval times, and overall bureaucracy have taken mattes into their own hands and passed right-to-try legislation (now available in 31 states and counting.) Where legal, individuals can completely circumvent the FDA and get access to an unapproved investigational medicine. The FDA must step in and educate the public about the risks involved. Most people don't know that 95 percent of investigational compounds fail in phase 1 clinical trials and 80 percent fail in phase 2 trails. Few if any investigational compounds have antidotes and their adverse events have the potential to be permanent.

Improve the collection and monitoring of safety and adverse event reports. The FDA is doing a poor job compiling adverse events and reporting them to health care professionals and the public. Adverse event tracking through the FDA Adverse Event Reporting System (FAERS) or MedWatch has the power to provide valuable real-time sharing of new drug safety issues that did not emerge during clinical trials. Unfortunately, the time-intensive process of reporting an adverse event to a drug company or the FDA is neither a requirement nor goal for prescribers, physicians, and pharmacists who are already burdened with overwhelming amounts of paperwork for insurance companies, Obamacare, and electronic medical record requirements.

Alert consumers about the abuses and dangers of mail-order pharmacies. Many patients are now required to get their medications via mail order rather than with the time-tested method of having a face-to-face relationship with a pharmacist. Almost all mail-order drugs come from the aforementioned "sweatshop" countries. Even more problematic, it is difficult to store mail-order drugs at the temperatures the FDA requires. Non-refrigerated prescription drugs are required to be kept at 68 and 78 degrees Fahrenheit.

When stored outside of this range, the drugs begin to denature and become inactive. Remember that the next time your mail-ordered medication is left in your mailbox during a heat wave or the dead of winter.

Arizona has one of the highest teen pregnancy rates in the country. One potentially obvious contributor could be the summer temperatures in the Sonoran Desert. It's definitely a bad idea for mail-order birth control drugs to cook in 100-degree-plus temperatures in aluminum mailboxes or the back of UPS delivery trucks, inactivating the active ingredients.

It's a mystery to me why the FDA and various state boards of pharmacies remain silent on this important issue. Summer broiled or winter frozen, temperature degraded prescription drugs represent an important public health issue.

These items are just my top ten. I, and other FDA watchers, could easily double, or even triple, the wish list. I recognize that higher priority issues with the incoming administration include the economy, the repeal of Obamacare, illegal immigration, and terrorism. But I still hope that Representative Tom Price, President-elect Donald Trump's choice to lead the Department of Health and Human Services, puts these many serious problems at the FDA under careful scrutiny.

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