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America Desperately Needs a Much Better F.D.A.

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In the early 1960s, an unflappable Food and Drug Administration scientist named Frances Kelsey spared the nation from the horrors of thalidomide. The drug had become popular around the world as a remedy for a variety of ailments, including morning sickness in pregnant women. Although there had not been many studies of its safety, thalidomide's manufacturers marketed it as exceedingly safe. Regulators in many countries, including Canada and across much of Europe, approved its sale.

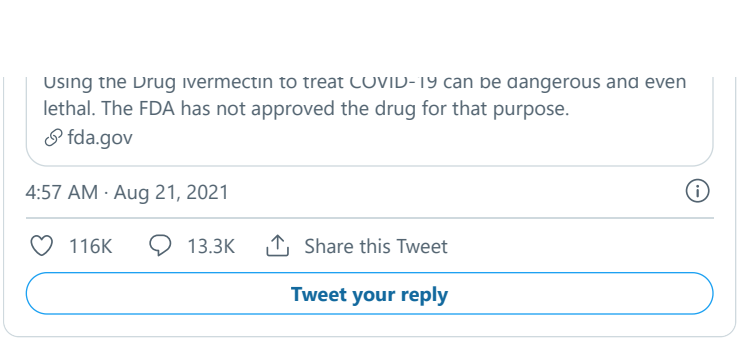
Thalidomide's American licensee had expected officials at the Food and Drug Administration to follow suit. But the application was assigned to Kelsey, a pharmacologist new to the agency who set an unusually high threshold for approval: She wanted to see thorough clinical evidence of thalidomide's safety.

For much of 1961, Kelsey repeatedly held up U.S. sales of the drug, each time demanding more data. The drugmaker's executives became irate and bombarded Kelsey and her bosses with letters and phone calls complaining of what they considered bureaucratic nit-picking.

Kelsey wouldn't budge. Thalidomide was kept off the American market. And in late 1961, when doctors in Europe began to link the drug to a wave of birth deformities, Kelsey's diligence was validated. Thalidomide was eventually blamed for causing birth defects in thousands of children around the world. Thanks to one heroic bureaucrat's insistence on strong clinical data, cases in the United States were estimated to be in the dozens. (Some 1,200 American doctors were offering the drug to patients through loosely run clinical trials sponsored by the drugmakers.)

Lately I have been wondering: What might Frances Kelsey think of today's F.D.A., an agency that has grown alarmingly cozy with the industry it is supposed to oversee? What would she make of Americans' deep mistrust of the drug companies it regulates? And how would she rate its performance on some of the most important health issues we face — its often confused response to the pandemic, its role in surging drug costs and, most damningly, the central role it played in accelerating the opioid epidemic?

I realize this is a tricky moment to criticize the F.D.A. We live in a conspiratorial age of meme medicine — an era when lots of people would rather take untested snake oil hawked by politicians, pundits and B-list celebrities than vaccines whose effectiveness and safety have been proved in clinical studies and that have been approved by the F.D.A. Calling attention to the agency's failures might only deepen distrust in the F.D.A. when its mission is more vital than ever — at the very least to remind Americans that they are not horses and should consequently refrain from taking horse medicine.



On the other hand, would as many Americans be resorting to veterinary medicine if over the years the F.D.A. had more successfully done its one job, inspiring trust in the safety and effectiveness of the drugs it regulates? Sure, there are lots of conspiracy theorists who will accept lunatic ideas no matter what the F.D.A. says or does. Still, if the drug industry and its regulators are mistrusted, one plausible reason is that they have not been doing a lot to inspire trust lately.

“What we’ve seen since the 1990s is an F.D.A. that has been putting industry interests consistently ahead of public health,” said Andrew Kolodny, an opioid policy researcher at Brandeis University who has studied how the agency’s failures contributed to the opioid crisis.

The F.D.A. is embroiled in a scandal over aducanumab, a $56,000-per-year Alzheimer’s drug that the agency approved even though an advisory panel of experts declined to endorse it because evidence that it worked wasn’t persuasive enough.

The aducanumab approval fits a worrying pattern: Since the 1980s, the F.D.A. has been approving more new drugs, at a faster pace and with fewer and weaker studies to support their safety and effectiveness. The agency has also been faulted for poor oversight of the clinical trials used to decide whether a drug is safe.

Both Donald Trump and President Biden have referred to F.D.A. approval as the “gold standard” of drug safety. It is a pretty tarnished gold. One-third of the drugs approved from 2001 to 2010 were found to have major safety issues years after approval, a study by researchers at the Yale School of Medicine found. The F.D.A. was once criticized for taking too long to approve drugs, but now it is much quicker to approve drugs than its European counterpart.

Why do regulators approve so many potentially dangerous drugs, when many provide only minor improvements on existing drugs? Part of the story may be the conflicts of interest baked into the structure of the F.D.A. In 1992, Congress allowed the agency to collect fees from the industry it oversees to pay for the high costs of drug approvals. These fees pay for much of the salaries of F.D.A. review workers responsible for the approval of new drugs.

The F.D.A.’s critics say the fees have turned the agency into more of a partner of the industry than an overseer. The fees are set by negotiation between the agency and the drug industry; negotiations set the amount the industry pays the agency and also set certain “performance goals” the agency must adhere to, among them commitments on the speed of its reviews.

In a 2017 paper on the effects of the F.D.A.’s industry funding, experts at Harvard Medical School wrote that “a focus on speed, flexibility and responsiveness to industry needs may accelerate approval, but it can also increase the chance that a newly marketed drug may not be as effective or safe as traditional standards would have demanded.”

Former employees have said the agency’s culture rewards workers who approve drugs over those who reject them. “You don’t survive as a senior official at the F.D.A. unless you’re pro-industry,” Thomas Marciniak, a former agency employee, told ProPublica in 2018.

And there is a lucrative reason to try to make it as a senior official at the F.D.A.: It could lead to a cushy second career as a consultant to the drug industry. The revolving door between the F.D.A. and the industry spins so fast, we could tap it as a source of renewable power. Between 2001 and 2010, according to one study, 26 F.D.A. reviewers who worked on cancer and hematology drugs left the agency; more than half of them went on to work or consult for the drug industry. Scott Gottlieb, who ran the agency from 2017 to 2019, is now on the board of directors of Pfizer.

This summer I read “Empire of Pain” by Patrick Radden Keefe of The New Yorker, a superb and infuriating investigation of the Sacklers, the family that owned the company that made the powerful and addictive painkiller OxyContin. Keefe — building upon work by other journalists who’ve investigated the opioid epidemic, including Barry Meier, a former New York Times reporter — tells a riveting story of a family business driven by greed and willfully blind to its igniting role in an epidemic that killed nearly 500,000 Americans from 1999 to 2019.

Before reading Keefe’s book, I had been under the impression that the F.D.A.’s initial approval of OxyContin and its long neglect of the dangers posed by opioids was a routine story of regulatory mishap — that the agency got it wrong because drugs are complex and unpredictable and regulators aren’t perfect.

But Keefe makes clear the F.D.A.’s mistakes were worse than simple incompetence. The Sacklers’ company, Purdue Pharma, cultivated close relationships with key F.D.A. officials. Among them was Curtis Wright, the F.D.A. official who oversaw the process for OxyContin’s review. At times during the review process for OxyContin, Keefe writes, “it could seem that Wright had given up his role as impartial

federal regulator and become a sort of in-house advocate for Purdue." Within two years of leaving the agency, Wright went to work for Purdue.

Can the F.D.A. be fixed? Perhaps, but it would take rare political courage to enact reforms that might address the agency's deepest problems, like its reliance on drug money to pay for its operations. Most of the political pressure on drug approvals runs in the direction of action; the pharmaceutical industry will always want to sell new products, and patient advocates tend to be desperate for new treatments even if there might be risks to safety.

Sometimes courageous scientists stand firm against these forces. In June, three F.D.A. advisers resigned in protest of the approval for aducanumab. On Tuesday, the agency said that Marion Gruber, the agency's vaccine director, and her deputy, Philip Krause, will soon leave the agency, reportedly in part because they were upset about the Biden administration's recent announcement that Americans should get Covid-19 booster shots.

Perhaps these resignations illustrate how far the agency has strayed from Frances Kelsey's day. Back then, a sole scientist could stand firm against industry and political pressure and make a difference for patients. Not anymore.

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