Scott Gottlieb Is Not a Free Market Firebrand

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It's mid-December, and Scott Gottlieb is at the Harvard Club. The Manhattan Institute has invited a few dozen people for an intimate discussion about what's happening at the Food and Drug Administration (FDA). As they eat finger foods and sip cocktails, a relaxed Gottlieb meanders around the room sans entourage and snags the occasional pretzel stick from a platter. As a former think tanker himself—he was an American Enterprise Institute resident fellow for roughly a decade—these are his people.

Everyone takes their seats. Gottlieb's old friend Peter Huber, an attorney and senior fellow at the host institute, is sitting right up front. Just a few years earlier, the two had partnered to argue the affirmative in a debate over whether "the FDA's caution is hazardous to our health." But now that Gottlieb is the head honcho at the agency, some libertarians who once considered him a fellow traveler are finding him a tough nut to crack.

When the floor opens for questions, one is about his plan to require cigarette manufacturers to lower the nicotine in their products to a "minimally or non-addictive level."

"You want to take the nicotine out of cigarettes," the audience member says, incredulous. "Do you also want to take the alcohol out of booze?"

"The FDA does not regulate alcohol products," Gottlieb responds.

"Well, thank God for that," the questioner says, before plopping into his seat.

The exchange demonstrates just one of the ways in which Gottlieb is not the person many onlookers anticipated. When Trump nominated him to be FDA commissioner in March 2017, conservatives and libertarians applauded his record of advocating market-based health care reforms, while liberals bemoaned his financial ties to the pharmaceutical industry and predicted death and destruction.

They were both wrong. Instead of a radical deregulator, he has turned out to be a cautious institutionalist, focused on ensuring that his agency lives up to its obligations without exceeding the limits of its authority. Yes, he is nudging the FDA toward streamlining its approval process and encouraging competition in the drug and device markets. But Gottlieb was never going to burn the FDA to the ground, and people who thought he would weren't paying attention to what he's been saying all along.

Shill

"Scott Gottlieb's fervor for deregulation could harm patients," warned a piece published on the health news site *STAT*shortly after his appointment. "Farewell to drug regulation? Trump nominates a 'bona-fide pharma shill' to head the FDA," complained a *Los Angeles Times* headline.

Gottlieb really is a longtime critic of the agency. At the Manhattan Institute, he speaks with the same polish he's demonstrated in hearings before Congress, repeating some of his favorite mantras: The FDA needs to "think differently" when it comes to biologic therapies and medical apps; "speed vs. safety" is a false choice the FDA doesn't have to make. At times he seems to channel a seminal 2012 essay he penned for *National Affairs,* titled "Changing the FDA's Culture," in which he bemoaned the agency's "excessive desire for certainty" and its "mistrust of the doctors who eventually prescribe medicines and the companies that market them."

Gottlieb has argued repeatedly for reforming the way the FDA handles many of its duties, in particular the approval pipeline for drugs and medical devices. His criticisms were rooted in experience: He worked for the agency twice during George W. Bush's presidency, first as a senior advisor to Commissioner Mark McClellan and then as the deputy commissioner for medical and scientific affairs under Commissioner Andrew C. von Eschenbach. And like nearly every FDA commissioner before him, he has practiced medicine, as an internist and faculty member at the New York University School of Medicine.

He also has extensive experience working with the drug companies he's now tasked with regulating. The federal disclosure form he filed with the U.S. Office of Government Ethics after his nomination listed board positions at Tivorsan Pharmaceuticals, Tolero Pharmaceuticals, GlaxoSmithKline, Glytec, and Daiichi Sankyo U.S., as well as consulting fees related to work at Bristol-Myers Squibb, Vertex Pharmaceuticals, and various investment firms.

All of which made him a prime target on the left. At his confirmation hearings, Senate Democrats suggested that elements of Gottlieb's background—particularly his corporate ties—disqualified him for the job. They depicted him as a crony for the drug industry, hell-bent on stripping the agency of its regulatory powers. Sen. Elizabeth Warren (D–Mass.) read aloud a passage from the *National Affairs* piece suggesting the agency had over-corrected in response to the thalidomide crisis, in which a sedative given to pregnant women in the 1950s as an off-label treatment for morning sickness resulted in thousands of babies being born with deformed limbs and other congenital disorders.

In his essay, Gottlieb argued that the scandal, which didn't reach U.S. shores thanks to concerns raised by an agency employee named Frances Kelsey, "fostered an idealization of the lone reviewer championing an issue of safety against the prevailing orthodoxies, especially when it meant taking on corporate interests." That is a core part of the agency's mission, of course—but the downside of a purely oppositional attitude is that the agency "has sometimes subordinated and neglected its other key obligation, which is to guide new medical innovations to market."

Gottlieb dedicated more than 5,000 words to reconciling these two obligations without denigrating the FDA or dismissing the severity of the thalidomide error. Warren was less charitable. She read aloud 22 of his words—the part about taking on corporate interests—and then lobbed this question: "Dr. Gottlieb, do you think the FDA puts too high a priority on championing safety and unborn babies?" (He dodged, noting that the "modern FDA does a very good job of ferreting out risk preclinically.")

Many folks on the right likewise assumed that upon taking office Gottlieb would implement the suggestions he had outlined in *National Affairs*, which ranged from demolishing some of the obstacles the FDA has erected to prevent U.S. patients from accessing drugs sold in Western Europe to relieving junior review staff of the burden of making decisions that are above their pay grades. Some libertarians likely hoped he would upend the entire clinical trial process, approving drugs that have been shown to be safe while allowing patients and doctors on the open market to determine their efficacy.

In this, they have been disappointed.

Moderate

From the very beginning, Gottlieb resisted many of the expectations heaped upon him. When pressed during his confirmation hearing on his ties to "big pharma," he responded that working on the drug development end had taught him about "the unpredictable nature of innovation" and reinforced for him "the need for an absolutely objective regulatory watchdog over this field." He'd been to the other side of the looking glass, he explained, and it had revealed just how important the FDA's role really is.

When we speak in January, he comes across like a technocratic wonk with a surprisingly deep commitment to public service. He is also remarkably consistent when communicating about what motivates him: addressing public health concerns and following the letter of the law.

"I know there's a lot of concern about the federal agencies regulating certain aspects and facts of medicine," he says. "As you probably know, looking back on my writing, I voiced that concern over the years." But "when it comes to controlled substances, it's very different. The Controlled Substances Act, the CSA, the law, gives the federal government very explicit authority to regulate aspects of how those drugs are prescribed.…The idea that it has a scheduling process, the idea that the law prescribes limits on how many refills you can give and how much you can dispense—that is a very clear expression from Congress that when it comes to controlled substances, they intended for federal agencies to play a more prominent role in how drugs are dispensed and used."

Even Gottlieb's *National Affairs* article, held up by so many as evidence that he was a firebrand, was widely misinterpreted. While the tone was unmistakably critical of the agency's culture, the remedies he proposed were relatively modest. He suggested that Congress could import some of the structural advantages of the European Medicines Agency, which relies on political appointees to make final approval decisions on new medical products. That, in turn, would free up career staff to focus on doing the science.

"If FDA reviewers were relieved of the political consequences of final approval decisions, they would have more confidence and freedom to innovate in how they measure risk and benefit," he wrote. "They could focus less attention on medical-practice decisions—an arena that is largely beyond their practical or legal purview—and focus more squarely on the science of defining risk and benefit, which is the work at which the agency's staff is most expert."

Such a change would alter the way the FDA operates, but it would make the agency no less capable of executing its regulatory mission. It might even improve it.

Market Advocate

Gottlieb took a lot of heat during his confirmation hearing over the price of prescription drugs. But contrary to misconceptions, the FDA doesn't have the authority to regulate prices. Not directly, anyway.

Gottlieb has long argued that the key to making medications more affordable is increasing the number of products on the market. When patients have more than one choice, pharmaceutical firms have to compete. The FDA has done its part to engender this competition by approving a record number of generic drug applications in two consecutive years. Fiscal year 2016 saw 651 generics receive full approval, while fiscal year 2017 saw 763.

The agency can't approve new generics, however, if generic manufacturers can't submit robust applications, which is why Gottlieb made a point early on of decrying anti-competitive industry practices that allow drug makers to protect patents long after they've expired.

"We know that sometimes our regulatory rules might be 'gamed' in ways that may delay generic drug approvals beyond the time frame the law intended, in order to reduce competition," Gottlieb wrote in a recent FDA blog post. "One example of such gaming is the increasing unavailability of certain branded products for comparative testing."

Most Americans are at least vaguely familiar with one example of this practice. In August 2015, a company called Turing Pharmaceuticals, led by CEO Martin Shkreli, bought the rights to a drug called Daraprim, which is used to treat a parasite that affects people with weakened immune systems. At the time of the purchase, the medicine was no longer protected by a patent. So when Turing raised the price of a single Daraprim pill from $13.50 to $750—generating a huge backlash and focusing critical attention on Shkreli, who was perfectly willing to play the part of a cartoon supervillain—many wondered why another company didn't simply undercut Turing's aggressive pricing scheme by releasing a generic version.

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The answer is that no company could seek FDA approval for a generic version, because Turing had put Daraprim under "restricted distribution," a designation—in this case, self-imposed—allowing drug makers to limit who can acquire their products, even when there's no post-market data suggesting the drug is dangerous.

If a drug is on restricted distribution, "then some other little company can't get samples of it," says Derek Lowe, a pharmaceutical researcher and author of a widely read blog on pharmaceutical development called *In the Pipeline*. "And if you can't get samples of the actual drugs that you're trying to compare your own generic against, you can't run a clinical trial for the FDA."

In March 2017, the House Committee on Oversight & Government Reform held a hearing to examine companies' misuse of this option. Later, Gottlieb became the first FDA commissioner to argue that the agency will do whatever it can to close the loophole—even if it can't do much.

"FDA is not the [Federal Trade Commission]," Gottlieb wrote in a blog post calling out restricted distribution. "It is the FTC's responsibility to prevent anticompetitive business practices. But Congress set out certain laws that are meant to strike a careful balance between pharmaceutical innovation and access to lower cost generic products, and FDA has an important responsibility to enforce those laws in a manner that adheres to the balance struck by Congress."

Demanding that branded drug owners comply with the spirit of federal regulations isn't a partisan issue. Both House Republicans and House Democrats have investigated it in the last decade. While free marketeers are often cast as being in the tank for corporations, this challenge highlights that being pro-market is not the same as being pro–big business. David A. Hyman, a law professor at Georgetown University and an adjunct scholar at the libertarian Cato Institute, recently argued in the journal *Regulation* that "the FDA should send a clear signal to pharmaceutical companies that anticompetitive behavior will not be tolerated." Gottlieb is doing just that.

Which makes sense: He views pharmaceutical firms as participants in a social contract. The government encourages them to innovate by giving them a lengthy monopoly on the medications they patent. In exchange for that protection, firms are expected to cooperate when the time comes to develop generic versions of their drugs. The right to monopoly has a corresponding responsibility, in other words, and Gottlieb has no patience for companies that shirk it.

While he might not be able to stop the next Martin Shkreli, Lowe is pleased to see Gottlieb put the issue front and center. "I'm applauding it," he says.

Regulator

In April 2017, all but four Senate Democrats voted against confirming Gottlieb as FDA commissioner because they assumed his ties to the pharmaceutical industry would prevent him from cracking down on opioid makers in the face of increasing overdose deaths. To the chagrin of some of Gottlieb's libertarian champions, that assumption has since been proven wrong.

Until recently, the agency played a bit part in the national drama, approving or rejecting pain treatments and—in rare circumstances—revoking approval after concerns arose. Gottlieb has embraced all of those powers while adopting an advocacy role that's new for the FDA.

Opioids were among the issues of contention at Gottlieb's confirmation hearing. "We need a leader at the FDA who recognizes the dangers of prescription painkillers, who will stand up to

big pharma and reform the FDA to prevent addiction before it takes hold," Sen. Ed Markey (D–Mass.) said at the time. "Dr. Scott Gottlieb is not that individual."

Gottlieb, it turns out, *is* that individual. A month later, with Gottlieb at the helm, the FDA publicly asked Endo Pharmaceuticals to pull one of its drugs off the market due to "dangerous unintended consequences."

First approved in 2006, Endo's Opana ER was reformulated in 2012 to be "abuse-deterrent." The reformulated version proved difficult to snort, but users found they could still inject it by scraping the coating off the pills, grinding them down, mixing the powder with high-proof alcohol, and pulling the solution into a syringe using a cotton filter.

Post-market data collected and reviewed by the FDA revealed that using the drug this way—via injection rather than inhalation or swallowing—correlated with the spread of HIV and hepatitis C. It was also linked to a potentially deadly clotting disorder. So the FDA gave Opana an option: Remove the drug from circulation voluntarily, or the FDA would begin the process of rescinding its approval.

The decision was widely applauded by health advocates who believe the FDA has been too lax for too long when it comes to dangerous opioids.

"He's performing better than I anticipated on the opioid front," says Andrew Kolodny, executive director of Physicians for Responsible Opioid Prescribing (PROP). "For example, he's been calling attention to over-prescribing of opioids as a key driver of the opioid epidemic, he's been pointing out that opioid addiction frequently develops from medical use, and he sought removal of Opana, an opioid that never should have been approved."

Kolodny adds that Gottlieb's decision to "embrace" a report from the National Academy of Sciences, which called on the agency to overhaul its opioid policies, suggests he "implicitly acknowledged that FDA has been making awful decisions about opioids for the past 20 years."

Some critics fault the agency for approving Purdue's OxyContin—the drug they claim started the modern opioid crisis—in 1995. More recently, they have zeroed in on the 2013 approval of a painkiller called Zohydro despite the drug's lack of abuse-deterrent features and the 2015 approval of OxyContin for children. (Testimony from pediatric oncologists indicated that kids with terminal cancer could benefit from that decision.)

Gottlieb's move against Opana was part of a bigger play. In October, he testified before a House committee that the FDA would soon take a series of additional steps intended to address the epidemic.

Free marketeers are often cast as being in the tank for corporations, but Gottlieb's harsh words for pharmaceutical companies highlight that being pro-market is not the same as being pro–big business.

In November, the agency released a 30-page guidance document formally defining "abuse-deterrent formulations" (ADFs). The idea is to help generic opioid makers replicate the features already used in patented painkillers—for example, chemical agents that cause crushed pills to

gum up when mixed with water—with the ultimate goal of completely eliminating abusable opioid drugs from the market.

"If a product had a higher propensity to be abused because of certain features, or if two products are the same but one has a higher propensity to be abused, that's something we should and do have the authority to take into consideration," Gottlieb says, when deciding whether to approve the drug.

There is evidence, however, that the 2010 release of abuse-deterrent OxyContin led nonmedical users to switch to heroin and fentanyl, which are far more dangerous than prescription opioids. The authors of a 2017 National Bureau of Economic Research paper concede that the reformulation may have reduced nonmedical use of the drug by 40 percent—but they also suspect that "the potential mortality gains from the reduction in OxyContin misuse" were eradicated by a marked *increase* in heroin-related deaths.

Emerging research that casts doubt on the net positive of abuse-deterrent formulations has caused some to wonder why Gottlieb is pursuing that avenue of reform so vigorously. "When I prescribe oxycodone or OxyContin to my surgical patients, they take it with a glass of water," says Jeffrey Singer, an Arizona surgeon and fellow at Cato. "I don't have to tell them, 'Don't snort it, don't try to inject it.' If someone really wanted to abuse an ADF version of OxyContin, they could just take a handful of them all at once."

"I think Gottlieb was a great pick, and his sensibilities are good," Singer adds. "But there's no other conclusion to come to: These formulations have unintended consequences." Then he pauses. "Gottlieb is a smart guy. He's got to be able to see this."

Deregulator

Fortunately, promoting abuse-deterrent formulations isn't the only facet of Gottlieb's opioid plan. According to the National Survey on Drug Use and Health, 75 percent of opioid misuse begins with opioids prescribed to someone other than the abuser. Because of that, Gottlieb says, "I think where we could have a particularly prominent impact is in trying to reduce the rate of new addictions."

One easy way to do that, he thinks, is by encouraging doctors to prescribe quantities of opioids that closely match a patient's situation: "So no more 30-day prescriptions for tooth extractions when that should really be a two- or three-day prescription." Ideally, this will leave fewer pills to fall into the hands of friends and family who aren't using them for medical reasons.

Gottlieb is also a vocal proponent of allowing opioid addicts to transition to medication-assisted therapy (MAT), which involves the use of opioid agonists such as methadone and buprenorphine that scratch the physical dependency itch without jeopardizing user health.

The value of such drugs is now accepted in the harm-reduction and legalization communities, but older policy makers in Washington still view them with suspicion. Asked about it last year, former Health and Human Services Secretary Tom Price told a West Virginia newspaper that it was "just substituting one opioid for another." Luckily, Gottlieb doesn't see it that way.

"We're trying to talk about the problem in a little bit of a different way than it's been talked about in the past," he says. "There's a perception among some that you're basically replacing one opioid with the other. But if you can help someone who is addicted to an opioid lead a life of sobriety by administering methadone or another MAT drug, you've treated the addiction. That is treating the addiction."

Gottlieb has expressed this sentiment to federal lawmakers, testifying in October that "clinical evidence shows that people may need treatment with medications for long periods of time to achieve a sustained recovery. Some may even need a lifetime of treatment."

Currently, quotas restrict how many patients a doctor can concurrently treat with buprenorphine and methadone. Because those numbers are set higher up the chain of command, by the Department of Health and Human Services, Gottlieb can't increase them himself. But the FDA did recently approve a new formulation of long-acting buprenorphine, a drug that provides milder opioid effects with less euphoria, called Sublocade. It requires just one injection a month to stave off cravings for drugs like heroin and OxyContin.

Gottlieb also revealed that the FDA will be convening a working group to expand the indications for MAT drugs, so that health care providers can initiate treatment outside of drug rehabilitation settings. By proactively reviewing evidence, he hopes his agency can help expand access—a first for the FDA.

"It is clear that Gottlieb actually understands what works to treat opioid addiction: long-term, sometimes lifelong, use of maintenance medications like methadone and buprenorphine," says Maia Szalavitz, a researcher and reporter whose work on addiction has been recognized by the American Psychological Association and the American College of Neuropsychopharmacology. "These two [medications] have been shown to cut the death rate by half or more," she adds—and Gottlieb "seems to really get why and how they work, unlike many, many people in this field. If FDA can get rid of the overregulation of methadone and buprenorphine, it would save lives."

Restrictionist

Gottlieb often tells people what the FDA *cannot* do: singlehandedly stop anti-competitive practices; lower drug prices by fiat. Yet he is eager to use what powers his agency does have, sometimes in controversial ways.

In November, he announced in a blog post that the FDA had "detained hundreds of shipments of kratom," an unregulated herbal supplement native to Thailand that a diverse group of Americans have recently come to value for its dual uses. A member of the coffee family, kratom has a mild stimulative effect at low doses, much like coffee or tea. Another alkaloid in the plant, however, acts on the opioid receptor, and at higher doses, the herb works as a mild sedative. So while some people use it as a substitute for caffeine, others have used kratom to wean themselves off prescription opioids.

Kratom is not nearly as powerful as commonly prescribed opioids (to say nothing of heroin or fentanyl), and based on mortality data, it is less dangerous than common cold medicines and many other nonprescription drugs. Like green tea and Tylenol, however, it can be toxic to the

liver at high doses, and the fact that it is unregulated means customers seldom know exactly what's in the formulations they buy.

In August 2016, the Drug Enforcement Administration (DEA) announced that it would use its emergency powers to place kratom in Schedule I, rendering it illegal to possess, use, sell, buy, or manufacture.

The backlash was immediate and intense. "There is no reason why hundreds of thousands of Americans who purchase kratom should be turned into criminals in three weeks," Susan Ash, director of the American Kratom Association, said in a statement. More than 120,000 people signed a petition opposing the pending ban. The agency eventually backed down.

But Gottlieb remains essentially unpersuaded by the popular outrage. "I understand that there's a lot of interest in the possibility for kratom to be used as a potential therapy for a range of disorders," he wrote. "But the FDA has a science-based obligation that supersedes popular trends and relies on evidence." If Americans are going to use kratom as medicine, he warned, the FDA is going to treat it like medicine.

He encouraged those who want to use the drug to "conduct the research that will help us better understand kratom's risk and benefit profile"—in effect demanding that they submit a new drug application and conduct clinical trials, which cost millions of dollars and last for years.

"In the meantime," he concluded, "based on the weight of the evidence, the FDA will continue to take action on these products in order to protect public health."

The available evidence suggests that on this issue, Gottlieb is evincing the same excessive cautiousness he once said characterized his agency's worst decisions. While there's no data pinpointing exactly how many Americans use kratom, the DEA says it encountered close to 12 million doses of the supplement between 2014 and 2016. Yet as of November 2017, the FDA could report only 44 cases in which a deceased person in the U.S. was found to have used kratom near the time of his or her death. Of those 44 cases, many involved the use of multiple drugs or involved people with pre-existing health issues. Far more people in the U.S. die from acetaminophen overdoses every year than are thought to have died from kratom ever.

Net Positive

So who is the real Scott Gottlieb? Contrary to widespread expectations on both sides of the political aisle, he is not an anti-regulation fundamentalist. The FDA's recent actions on prescription opioids, tobacco, and kratom—to name but a handful of stern regulatory actions the agency has taken in the last 10 months—make it hard to avoid the conclusion that he really does embrace the FDA's mission.

Most of all, Gottlieb appears to be a follower of protocol—someone who makes decisions less because of a personal ideological orientation and more because of the powers and purview the agency already has. "I spent a decade writing about my concerns with the federal government regulating the practice of medicine, and I still feel that way," Gottlieb said at the Manhattan

Institute event. "But if you look at the pharmaceutical industry, there's no space that Congress has given more clear instructions on how to regulate."

Even in cases where Gottlieb has interpreted his mandate in ways that advance freedom, his reasoning has been measured and fundamentally conservative. When the FDA repealed Obama-era regulations limiting what we can learn about ourselves from direct-to-consumer genetic testing kits such as 23andMe, Gottlieb did not argue that the government has no right to police what we can learn from our genes. Instead, he said that making such information available will help "people to make more informed lifestyle choices." It was a public health play, not an ode to negative rights.

Still, at a time when federal agency heads seem to be operating with precious little oversight from the White House, Gottlieb's modesty—even if it's feigned—is reassuring. Unlike, say, Ben Carson, whose time heading the Department of Housing and Urban Development has been marked by directionlessness, or Attorney General Jeff Sessions, who has abandoned the reforms pursued by his predecessors, Gottlieb has both a sense of purpose and a sense of limits.

He has chosen to focus his reformist energies on a handful of discrete policy areas where groundwork had already been laid, betting that thoughtful, stepwise changes will have more staying power than a radical rethinking of the agency's scope and mission would. And he has scored some wins worth celebrating along the way.

Since 1976, for example, makers of health care technology have been required by the FDA to test their products against previously approved predicate devices. While this has historically worked all right for processing products that are marginally better iterations of those from a generation or two earlier, the rules don't account for the leaps and bounds the private sector is capable of making, or for the entirely new paradigm that would be needed to effectively govern software. The idea of a device "updating" its own operating system would have sounded incomprehensible when this regulatory guidance was written, and yet it's how most consumer gadgets now work. Under Gottlieb, the FDA's medical devices division is working on new regulations that will help expedite the approval of technology that is safe and effective, even if it functions in a novel way.

Yet by nature, Gottlieb seems reluctant to take credit for some of the FDA's biggest accomplishments during his tenure. "We were going to have a record year for generic drug approvals regardless of whether I arrived in FDA or not," he says.

That kind of modest stewardship feels downright unfashionable in an era of political and ideological polarization. For critics of the drug industry, Gottlieb will likely seem too lenient; for desperate patients, too cautious; for individualists, too overbearing. Even his admirers can likely imagine things they'd have him do differently. But in many ways, he is exactly what he always claimed to be.

"You can't come into an organization like this, with a very high-caliber professional staff—people who have been working on issues for many years—and just sort of hand out pieces of paper that are going to create new policy and command implementation," he says. "I think what

you try to do is set an overall direction. You come in with policy goals, and you leave it, in some respects, to the staff to try to come up with the specific policies."