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She Didn't Need To Be Commissioner: Janet Woodcock's Transformative Legacy

by Sarah Karlin-Smith

She is as polarizing as she is powerful, but whether you think Janet Woodcock is drug development's hero or public health's enemy, there's no denying she dramatically transformed the US FDA over her 35-year career.

After a 35-year career, Janet Woodcock is expected to wind down her time at the US Food and Drug Administration in 2022 having never held the agency's most senior role – commissioner – permanently. But that hasn't stopped her from being one of the most powerful forces in modern drug regulation, and in fact may have been what kept her so influential for such a long period of time.

Unlike a commissioner, Woodcock's period of leadership wasn't limited to a few years, and her other FDA posts came with the unique ability to make changes that might have actually been harder for a commissioner.

The joke more than a few interviewees made for this retrospective of her career is that Woodcock was often in some ways the de facto agency head – at least when it came to the pharmaceutical industry.

More than two decades of Woodcock's agency tenure were spent as the head of the Center for Drug Evaluation and Research, where FDA experts say she often had little-checked authority to enact her agenda independent of the agency's constantly varying political leadership and even the US Congress.

While there are many long-time champions of Woodcock, including several in the drug industry, who are no doubt disappointed President Joe Biden decided against nominating her for the permanent commissioner role after filling in as his acting commissioner for about 10 months, there's a case to be made that she already ceded the post with the most influence over the pharma sector.

"Even had she become commissioner, I think she would have been diminished in her power relative to her tenure at CDER," said Daniel Carpenter, the Freed Professor of Government at Harvard University who has studied the history of the FDA.

Carpenter argued Woodcock's career is a demonstration of a phenomena political scientists and scholars of public administration have been writing about for decades: the power of managerial, long-tenured civil servants.

One reason for Woodcock's unusual amount of power even beyond that of other senior civil servants is the drug center's unique reliance on industry-supplied user fees instead of taxpayer dollars. In fiscal year 2020 for example, *CDER's budget was $1.73bn*, of which 28% ($508m) came from taxpayer dollars funded by Congress, while $1.25 bn or 72% came from user fees for prescription drugs, generic drugs, biosimilars and outsourcing facilities.

The agency and drug companies negotiate user fee agreements largely in private, determining how much money CDER will get for a variety of programs and for what purposes such funds can be used with little Congressional oversight.

"Even though Congress does have to approve the final legislation, it's often presented as *a fait acompli*," Carpenter said. "So what that means is that people who work under these budgets don't have to answer to Congress or don't have to answer to Congress as much for what they do. The power of the purse at some level, which is an Article One constitutional power, has been greatly reduced in the case of drug regulation," Carpenter said.

In Woodcock's case, FDA experts say she not only needed to rely less on Congress for funding as some other government agency officials do, but also less on the FDA commissioner's office and it choosing to fund her priorities as well. This made it easier for her to disagree with both of these points of power.

'Nobody Told Her What To Do'

Woodcock's long tenure, the respect she has gained throughout that time across the political spectrum, and her ability to be persuasive without appearing domineering has allowed her much autonomy from more senior officials.

She "doesn't raise her voice … she was in command of the room because she was always the most knowledgeable person in the room, she had the best grasp of the facts," said Stacy Cline Amin, a partner at Morrison & Foerster, who served as FDA chief counsel from 2018 to 2021 and also interacted with Woodcock in other government roles, including when Amin served as chief counsel of the Senate Health, Education, Labor and Pensions Committee.

"Nobody told her what to do … even the Secretary wouldn't try to tell Janet Woodcock what to

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do," Amin said. "It was always more of a conversation with her or a negotiation with her. ... She could really see the big picture and was great at shaping reasonable outcomes to challenging situations."

She didn't get rattled, even in tense meetings, Amin added, such as when dealing with the longest government shutdown in history in late 2018 and early 2019, or during the early chaotic days of the COVID-19 pandemic.

Woodcock said her calm demeanor was the most important quality she brought to the role of acting commissioner during the COVID-19 pandemic.

"The more crises escalate, the calmer I get. And so I'm able to lead under fire," Woodcock said in late November at the Biopharma Virtual Congress run by Prevision Policy and Friends of Cancer Research.

Every Commissioner Needs a Truthteller

Woodcock's calm demeanor shouldn't be confused with timidity. On the contrary, she is well known for being direct and unafraid to disagree, including with her superiors.

"I think it's one of her greatest qualities that she has the strength of character to be honest and direct and forthright," said Andrew von Eschenbach, who served as FDA commissioner from 2006 through early 2009.

Some people, von Eschenbach said, misinterpret that aspect of her character, as she doesn't come across as "warm and fuzzy" or the "most politically astute person on the planet."

But von Eschenbach found her directness invaluable.

"You need people to tell you the truth in Washington," he said.

Jane Henney, who served as FDA commissioner from 1999 through early 2001, expressed a similar sentiment, saying one of the reasons she enjoyed working with Woodcock was her forthrightness.

"You don't always come to the same place in terms of issues, but you can have a very healthy disagreement with Janet, a respectful disagreement with Janet. And I just think that's something that any commissioner needed was that truthteller, the one who could say, 'I think we're going down the wrong path here,' or 'we could approach something differently' and give you innovative and creative ideas," Henney said.

"I just always counted on her candor to keep everybody, including me, honest because you might

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not ask for it, but you were going to get it."

"Culturally, FDA is not a place that encourages confrontation," said Howard Sklamberg, a partner at Arnold & Porter and a former FDA deputy commissioner. But Woodcock is "aggressive," he said, adding this characterization wasn't meant to be negative. "She questions assumptions" and has a depth of knowledge across disciplines that many other managers don't have, so she doesn't have to defer to others.

An interaction with Woodcock, Sklamberg said, could sometimes feel like being in front of a judge.

"When you had a meeting with her you had to prepare in a way, frankly, you didn't for a lot of other FDA officials, because pretty much anything touching on drugs she knew."

Another strength of Woodcock's, a former colleague said, is she wasn't afraid to change positions when the evidence changed.

"People always say they want regulatory certainty. Which is true, except science is not certain, it's always evolving," said the former colleague. "So when you're a science-based regulatory agency you can provide regulatory clarity … but the certainty will always evolve based on how the sciences evolves."

When changing circumstances called for changes in policy, "sometimes you might have folks get caught up in the ego of, well I don't want to look like I'm changing my mind," the former colleague noted. "I don't know that, that has ever given Janet pause. And that takes pretty good strength of character, as well as confidence in what you're doing, but is probably also essential for someone with her tenure at the agency."

Agent Of Change

"FDA is sometimes slow to change," because so many people have to agree for change to happen, Sklamberg said, and some people just give up rather than keep pushing.

But Woodcock was very willing to revisit ways of doing things and was constantly questioning.

"In a way you can call her a disruptor," Sklamberg said.

Woodcock said this ability to change and improve a wide array of FDA programs and operations was one of the most rewarding parts of her career.

"I'm an innovator of new ways of doing things and moving with the science and moving with the times. And I think that's the role I've most enjoyed is being a change agent and actually making

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those things happen," Woodcock said at the Biopharma Congress.

> *"I feel like the greatest thing I could do is build an organization that can change and adapt, because science changes so rapidly and matters change rapidly," Woodcock said of FDA.*

Not pushing for change fast enough early in her career was one of her biggest regrets.

"You try to accommodate people, you try not to get people too distressed or disturbed and yet, if something needs to be done, it needs to be done. … What I regret is early in my career, as a manager, I didn't move things as fast as certainly I'm willing to do now, because I've learned the consequences of that. And if you have to make change, you just have to be straightforward and go ahead with it," Woodcock said.

"I feel like the greatest thing I could do is build an organization that can change and adapt, because science changes so rapidly and matters change rapidly," she said.

"Look at the pandemic. Nobody could predict this was going to happen and yet the center was able to deal with supply chain issues and with the huge influx of [investigational new drug applications] and [emergency use authorizations] and so forth. There were so many issues. They even turned distilleries into hand sanitizer manufacturers."

Was The Power Used For Good?

While there is almost no debate about the power and influence Woodcock commanded during her time at CDER, there is strong disagreement over whom and what that power has benefited and whom it may have harmed.

On the one side, there are her champions, who feel she harnesses the user fee era for good – modernizing a slow, outdated and underfunded agency into one capable of keeping up with the latest science and technological developments and providing industry with the guidance and regulatory certainty needed to get new treatments to patients quicker than ever before.

On the opposing side are her critics, who assert she has taken an agency meant to serve as a protector of public health by independently weeding out the snake oil from the cures and allowed it to trade its watchdog status for partnerships with the businesses it regulates, too often clearing poorly vetted medicines that haven't yet proven their true benefit to patients for the sake of putting hope and financial interests over sound science.

That coziness with industry has created an added burden for the health care system, argued Diana Zuckerman, president of the National Center for Health Research, because companies are often getting off the hook for certain kinds of evidence they used to have to provide to FDA because it is seen as too burdensome.

As a result, "doctors and patients have to make decisions about treatments based on much less information," Zuckerman said, which also leads to a huge strain on payers, particularly when this uncertainty comes with the high price tags of many new drugs.

Harvard's Carpenter said you can't fully fault Woodcock for the circumstances created by the user fee agreements. She did not invent the concept. But because of these agreements she created a new culture between FDA and industry that is not always well received.

> ***"It's important to recognize that while Woodcock has been a deregulatory force at the agency, the moves she made plausibly kept some of the most extreme anti-regulatory forces at bay, or at least neutered some of their arguments," Harvard FDA historian Daniel Carpenter said.***

Woodcock operated within a context where there was mainstream pressure to get medicines approved more quickly – an environment that wasn't necessarily one of her own making, Carpenter said.

Given that environment, where there were often libertarian-influenced pushes to weaken the FDA's role – some who wanted the FDA to basically allow everything on the market with some kind of ranking system on the safety and efficacy of products to help guide use – Carpenter says

she deserves some credit for preventing FDA from becoming a "Good Housekeeping seal of approval," noting she was able to keep many traditional structures intact and in some areas even foster improvements such as in clinical trial design.

"I think it's important to recognize that while Woodcock has been a deregulatory force at the agency, the moves she made plausibly kept some of the most extreme anti-regulatory forces at bay, or at least neutered some of their arguments," Carpenter said.

Approvals As Protection For Future Innovation

Still, Carpenter faults her for some changes in agency thinking and operations that he sees as detrimental.

A key criticism "is that she began to think about the drug review process as one in which the incentives and culture for future innovations had to be protected," Carpenter said.

"She began to consciously violate the independence of one drug review decision from another," he maintained, taking into account how FDA's decision to approve or deny one product might impact the entire field of development, instead of evaluating each application on its own merits of safety and effectiveness.

Carpenter said he isn't sure that this is illegal, but "it's definitely not in keeping with the spirit of the 1938 Food, Drug and Cosmetic Act, to tether these decisions, basically give one drug a pass so that somehow you think that there will be better incentives for developing others in the future."

The most high-profile example of this philosophy in action was Woodcock's approval of *Sarepta Therapeutics, Inc.*'s Duchene muscular dystrophy drug Exondys 51 (eteplirsen) over objections from the primary review team.

Woodcock argued the drug needed to be approved to ensure the continued financial viability of the company as well as continued drug development for the rare disease (Also see "*Woodcock's Consideration of Sarepta Financial Issues Raises Eyebrows*" - Pink Sheet, 19 Sep, 2016.)

"There's no evidence in the social science literature that says, 'oh, if you let one drug through, that's kind of iffy, all of a sudden, you're going to get a lot of other therapies, and they're going to be really good,'" Carpenter said.

The Sarepta decision was arguably the most controversial agency approval in recent years – until the 2021 approval of *Biogen, Inc.* and *Eisai Co., Ltd.*'s Alzheimer's treatment Aduhelm (aducanumab-avwa) over resounding objections from the FDA's independent advisors due to questions about the drug's benefits and safety profile.

Not only did the FDA approve the drug, but it also unexpectedly shifted course at the last minute and employed accelerated approval, despite previous agency assertions that the biomarker used in the study was not appropriate for the pathway.

The FDA then gave the drug a broad label that didn't match the population studied in clinical trials. (Also see "*Biogen Gets 'Almost Shockingly Broad' Label For Alzheimer's Drug Aducanumab*" - Pink Sheet, 7 Jun, 2021.)

Those surprising decisions capped off an already controversial review process given how closely the FDA was seen as working with Biogen to help get the drug across the finish line. (Also see "*USA FDA Gives Biogen Big Hand In Effort To Get Its Alzheimer's Treatment On The Market*" - Pink Sheet, 4 Nov, 2020.)

For Carpenter, these decisions reflect the FDA's and Woodcock's willingness to bend approval requirements as they see fit, even in the absence of clear, legally granted permission to do so. What's more, he finds it concerning that extra flexibilities had to be taken even though there are many exceptions to the traditional approval rules already written into law, such as the accelerated approval pathway, breakthrough designation and compassionate use.

"At some point, you have to ask, well, what do the standards matter anymore if we're creating exceptions – loophole after loophole after loophole?"

Woodcock critics fault her for encouraging the creation of the legal exceptions.

Zuckerman and other critics of Woodcock acknowledge a senior leader like her would often be divorced from most day-to-day drug review and approval decisions, but they argue she has refused to use her leadership position to set the tighter boundaries and standards they feel could have led to higher quality approvals during her tenure.

For example, Michael Carome, director of Public Citizen's Health Research Group, pointed to Woodcock's rejection of his organization's idea in the wake of the Aduhelm controversy that the FDA setup a firewall between agency staff who provide pre-submission advice on a drug development program and those who review the application (Also see "*US FDA's Woodcock Rejects Firewall Between Presubmission Advice And Application Review*" - Pink Sheet, 18 Feb, 2021.)

She "just outright rejected" the concept of maintaining a separation, Carome said, and instead "extolled the benefits of these collaborations."

Woodcock "really seems blind to how these collaborations could undermine the adequacy and integrity of the review," he said.

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Without FDA-Industry Collaboration, Everyone Would Lose

Woodcock's champions say that critics fail to appreciate the necessity of FDA-industry collaboration and that the critics misinterpret interaction with inappropriate behavior.

"Enabling innovation and enabling and creating transparency around pathways that industry can bring innovation to patients doesn't mean coziness with industry, it doesn't mean lessening standards. What it means is that there's clarity around the path forward," said Stephen Hahn, Donald Trump's second FDA commissioner.

"Janet is very pragmatic and open to finding ways to facilitate innovation. But make no mistake about it, that does not mean a lack of rigor around the assessment or a loosening of the standards," Hahn said.

> ***"The worst thing that we could do to patients is for developers to be spending hundreds and millions of dollars and developing a drug in the wrong way," former FDA Commissioner von Eschenbach said on the need for agency and industry collaboration.***

Von Eschenbach said that collaboration actually encourages better oversight. "To be a really wise regulator you have to be engaged in the total lifecycle of the product that you are developing. We recognized that it was helpful for FDA to have frequent meetings with drug developers as they were going through the process of that development so that we could understand what they were doing, and they could get appropriate guidance."

"The worst thing that we could do to patients is for developers to be spending hundreds and millions of dollars and developing a drug in the wrong way," von Eschenbach added.

Steven Galson, who served as deputy director and then director of CDER in the mid-2000s and spent a little over a decade with *Amgen, Inc.* starting in 2010, made a similar comment.

"I was fond of saying when I was at the agency that if a drug isn't approved by FDA after a 10-

year development process or more, it represents a communication failure. Something has gone wrong. Nobody really wants a surprise at the end of the process," said Galson, who currently serves on the board of directors of *BioCryst Pharmaceuticals, Inc.*.

The systems Woodcock put in place have left industry happier and patients better off, he said, because they're seeing access to products earlier than they would otherwise.

"I think the 'too cozy with industry' criticism overlooks the reality that to be a science-based regulator, you have to keep pace with the science. And the science is not always happening at a .gov email address. It's just not," said one former colleague.

"We don't want our regulators to be blind and deaf to what's happening in the outside world."

A third former FDA commissioner, Mark McClellan, who served from 2002 through 2004, also argued that the data are on Woodcock's side in terms of the industry-agency interaction generally leading to faster approvals without negative consequences.

The "substantial base of studies" on the user fee era have shown that these programs "significantly reduced time to development without immediately increasing unsafe drugs on the market. And conversely, leading to big improvements in patient health as a result," McClellan said.

"In an ideal world, we'd have enough government appropriations to fully fund the FDA without user fees, but we don't. And given that, she's done a great job of expanding a whole range of programs to improve regulatory science, enable more rapid scientific progress without compromising and in many cases enhancing FDA safety standards," he added.

Jim Greenwood, who recently stepped down as the CEO of the Biotechnology Innovation Organization, argued many of Woodcock's detractors fail to appreciate the incremental nature of science and drug development and the value those advancements can bring to patients.

"The way science works, it's not usually the case that all of a sudden somebody pops up with a cure to everything. … So whenever you can get something approved that's incrementally better than nothing, than what's available now, I think it's a tough decision to tell patients they can't have access," Greenwood said.

Woodcock herself talked at the recent Biopharma Congress about how many cancer patients are alive because they are able to live from one accelerated approval to another.

Soft Power

Those who worked with Woodcock directly at the FDA say the public also may not appreciate

how Woodcock used her relationship and respect from the industry to ensure compliance with regulations.

"I never saw her hands-on approach with industry as being tilted one way or the other, because people don't see the other side of it," Sklamberg said.

"She was very, very good at exercising … what you might call soft power. The agency has formal compliance processes, it can issue complete response letters, it can issue warning letters, can do all kinds of things. And it would do that. But sometimes when something wasn't getting done, she would pick up the phone. And she would call the leadership of a company or a CEO and say, I need you to take care of this problem. And that would get the problem solved, get a company to devote resources to a compliance issue. And she would not be afraid to do that. And she used that soft power both judiciously and effectively."

Those kinds of conversations were very powerful and often far more effective than issuing a warning letter, Sklamberg said.

Henney argued that Woodcock is popular with industry not so much because she did what they wanted but because she was consistent and even-handed.

Industry "could count on her candor with them," Henney said. "They could know that she was always solidly grounded in both the law and in science when she would make her decisions. And, you know, that's a terrific thing."

Woodcock: 'They Don't See The Big Picture'

Woodcock argues that many of her detractors focus largely on a few specific approval decisions they didn't agree with and ignore that on the whole the drug approval process has gotten more stringent under her watch.

"I believe that there's no comparison between the kind of drug review and the standards we had before I took over [CDER] and what we have now," Woodcock said in an interview with *Pink Sheet*, citing the increased level of professional scrutiny and improved systems for drug review.

She rattled off a litany of safety programs she spearheaded over the years including:

- Introducing the concept of risk management and developing Risk Evaluation and Mitigation Strategies (REMS) to help ensure the safe use of drugs that might otherwise be deemed too dangerous to approve;

- Building the first digital adverse event reporting system in the 1990s; and then later

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- The Sentinel system, an active rather than passive safety reporting system that is also one of the first-ever, real-world evidence systems.

Woodcock also started the Office of Surveillance and Epidemiology at CDER and created much more rigorous toxicology requirements for medicines.

"We really don't have the same kind of drug safety issues that we had when I started at CDER because we have established algorithms during drug development to test for those," Woodcock said. The number of drug recalls has also gone down over the years, she added.

Like many of her supporters, she argues that the FDA's involvement with industry is necessary to protect patients.

"We have to interact with industry, otherwise they would be going off doing trials and we will not accept them," harming the patients who "are putting their bodies at stake in these trials," Woodcock said.

Furthermore, she said that being "hostile to the people you regulate" is "not a professional attitude."

She acknowledged that "there's a lot to criticize about what I've done," but that lower drug approval standards are not one of them.

Woodcock also argues that with many of the FDA's decisions, including the controversial ones, there is no clear right or wrong answer and that is what makes the agency so vulnerable to criticism.

"FDA is always working within an area of uncertainty, so there's some judgment involved as well. If we just could implement the law and everything was crystal clear, then we wouldn't need doctors, right? You could just have a bunch of people, clerks or whatever, we wouldn't need doctors and scientists. But there's always a tremendous amount of uncertainty, and therefore there has to be some judgment," Woodcock said.

"I'm not an ideologue, I take this on a professional basis, not on a left or right wing, not on a political basis. So that's my response. I don't think they see the big picture," Woodcock said.

'She's Just Not In Her Little Golden Cage of the Agency'

Woodcock's supporters credit her with making the FDA more accessible and understandable to a wide range of stakeholders, not just industry.

One of Woodcock's achievements has been interacting more with all parts of the community

impacted by drug development, including companies, academics and patient groups, said Ellen Siegel, chairperson and founder of Friends of Cancer Research.

Fifteen or 16 years ago, the FDA was a "big black box to many people," Siegel said, and the FDA "was very isolated."

Woodcock opened the agency and was interested in hearing from all different groups, even those that disagreed with her.

"I think the fact that she can get out of the bureaucratic mindset of 'stay safe, don't talk to anyone' is really important," said Siegel, who noted Woodcock has also encouraged that of others at the FDA.

"Even people that don't agree with her respect the fact that she will listen, and she will debate and even argue, so she's just not in her little golden cage of the agency."

And like Sklamberg, Siegel argues Woodcock is not afraid to criticize industry when she feels it's necessary, pointing to Woodcock's complaint that both drug companies and academia tend to conduct duplicative or small trials that waste resources, including patients' time and energy, as one example.

Key Accomplishments

Beyond her work on drug safety, Woodcock can quickly list nearly a dozen major achievements during her time at the FDA.

Many people probably don't appreciate the full scope of her impact, former commissioner Henney said, because "many of the ideas that a commissioner or one or two of us got credit for, really a lot of those ideas spun out of Janet's head. She would see things, see opportunities to make improvements in the system to make it open and flexible, yet rigorous. And I just think that I can't say enough good things about what she's done at the agency, for the agency, for the public health."

Woodcock credited some of her work on international harmonization and advanced manufacturing improvements with ensuring the US and the world were better prepared during the COVID-19 pandemic.

She mentioned negotiating the first generic drug user fee agreement after multiple failed attempts, along with pushing Congress to create the biosimilar pathway and the biosimilar user fee program.

Other highlights she focused on were championing pharmacogenomics and individualized

therapies in the early 2000s, introducing the concept of patient-focused drug development, and revamping pharmaceutical quality for the 21st century, including creating an office focused on the topic at the FDA.

She also navigated the agency through several crises, like the contaminated heparin crisis in the late 2000s and a nationwide outbreak of fungal meningitis in 2012 caused by problematic compounding practices at the New England Compounding Center.

During COVID-19, she led the government's therapeutic development work before assuming the acting commissioner post.

She has so many various FDA programs and initiatives to her credit that perhaps even she can't remember them all.

One that is frequently mentioned by former colleagues is the Critical Path Initiative. Launched in 2004, it helped diagnose the reason for widening gaps between scientific discoveries and their translation into medical products. It led to a public-private partnership that works to accelerate the pace and reduce the costs of medical product development through the creation of new data standards, measurement standards and methods standards, known as drug development tools.

Opioids Cost Her The Commissionership

A primary reason for Woodcock losing out on the permanent commissioner nomination under Biden is due to a small group of lawmakers who feel her role in presiding over the drug center during the opioid crisis disqualifies her. (Also see "*Campaign Against Woodcock's US FDA Commissioner Bid Has Begun*" - Pink Sheet, 28 Jan, 2021.)

While Woodcock likely could have easily mustered enough votes in the Senate to clinch the job thanks to her bipartisan appeal, the Biden team was reluctant to name an FDA leader that would aggravate members of its own party – particularly Sen. Joe Manchin, D-W.V., whom the Biden team needs to appease to keep key parts of its Congressional agenda in play.

The White House's eventual pick, former commissioner Robert Califf, has also been criticized by Manchin for not doing enough about opioids, but the fact that he had already been vetted and confirmed by the Senate with 89 votes five years ago likely gave the administration the comfort level it needed. And nominating Califf when Biden did allows Woodcock to remain acting commissioner during the confirmation process.

On opioids, it is difficult to say exactly how much, if any, responsibility for the country's addiction crisis should go to Woodcock given that she was not solely responsible for the FDA's action and there is general agreement that the causes of the epidemic are multifactorial, with blame also falling on drug companies, doctors, and the illicit drug sphere among other actors and

societal factors.

Harvard's Carpenter said that while the opioid crisis is in part about the FDA, he isn't sure the FDA could have stopped it, given the agency's limited ability to control providers' behavior.

"They implicitly regulate the practice of medicine but their powers … are really, really limited," he said.

Others who worked in senior positions with Woodcock highlighted the impossible situation for the FDA, since any limits on opioids aimed at reducing abuse would also end up denying access to some patients in genuine need of pain relief.

The FDA was quick to jump on the wrongful promotion of opioids under Woodcock, they argued, and suggested that because of the severe mental health problems in this country, a drug abuse problem likely would exist regardless of what prescription medications the agency approved.

But critics say that even if the FDA should be given a pass for some of its early decisions on opioids, or seen as just one problematic actor among many, there is no getting around that the drug center under Woodcock's leadership has been too slow to change gears.

> ***"This isn't an individual who is saying, 'yes, we've made mistakes and we've corrected them,' or 'yes, we've made mistakes and we're going to correct them,'" Brandeis' Andrew Kolodny said of Woodcock's view on FDA's opioid policy. "She's someone who has really defended awful decisions that have led to loss of life."***

Notably, the agency continued to approve highly potent new opioids in the midst of the epidemic, such as the 2013 approval of Zohydro ER and its 2018 approval of Dsuvia, while its attempts to limit abuse by approving abuse-deterrent formulations have largely fallen flat and in some cases, like that of *Endo International plc*'s Opana ER, actually made the situation worse. (Also see "*US FDA Strategy On Abuse-Deterrent Opioids Needs Rethinking, Panelists Say*" - Pink Sheet, 15 Mar, 2017.)

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Andrew Kolodny, the medical director of opioid policy research at the Heller School for Social Policy and Management at Brandeis, pointed to a *2020 letter* Woodcock wrote in response to concerns of Sens. Maggie Hassan, D-N.H., and Ed Markey, D-Mass., as continued evidence that Woodcock doesn't appreciate the scope of the FDA's mistakes in the opioid arena. Instead, he sees someone who continues to defend past decisions.

For example, Woodcock wrote, "As we look back on our regulatory processes and decisions leading up to the opioid crisis, we can assure you that FDA followed the relevant rules and regulations, making decisions based on the best available data."

"This isn't an individual who is saying, 'yes, we've made mistakes and we've corrected them,' or 'yes, we've made mistakes and we're going to correct them,'" Kolodny said. "She's someone who has really defended awful decisions that have led to loss of life."

Kolodny argues that the FDA has long deflected the blame for the opioid crisis to people who misuse or abuse the drugs. But he argues that even early on, infamous opioids like OxyContin were disproportionately harming patients who were using the medicine as directed by the label.

Kolodny also points to Woodcock's treatment of Bob Rappaport, who retired from the FDA in 2014 after 20 years with the agency, the last 12 as the director of CDER's anesthesia, analgesia and addiction products division, which was responsible for reviewing opioid medicines, as an indication Woodcock is too comfortable with the agency collaborating with industry, including companies responsible for many transgressions during the opioid crisis.

Rappaport was involved in a high-profile, public-private partnership between the FDA, academia and industry related to the development of pain medicines that was the subject of "pay to play" allegations as drug makers were paying as much as $25,000 to attend the invitation-only meetings run by the group, where the FDA and other stakeholders discussed the best way to design, execute and interpret clinical trials for analgesics. (Also see "*FDA/Industry Interactions Might Get Revised Rules Of Road After Opioid Publicity*" - Pink Sheet, 14 Oct, 2013.)

Prior to his retirement, Woodcock awarded Rappaport an FDA Lifetime Achievement Award.

"If she had been interested at all in firewalls or in ways of preventing the industry from influencing FDA, you don't give an award to someone involved in a scandal for being too close to industry. You fire them or you try to fire them, you certainly don't praise them," Kolodny argued.

Woodcock's supporters maintain that in a multi-decade career there are bound to be decisions that aren't universally popular, particularly in a field where calls aren't always clear cut.

"Reasonable people can disagree about how quickly FDA can approve products, how you weigh

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safety, risk, benefit," Sklamberg said.

"FDA has to do the best that it can with the information it has and the statutes it has to operate within – the statutes are not always perfect," Amin said.

"People think science is black and white, but it has a lot of gray," Galson said. "And one thing about Janet is that she has made very, very tough decisions. She doesn't just delay things, and then she communicates why she's made the decision."

'In Order To Do My Job Effectively, You Have To Be Able To Empty the Bedpans'

Beyond the memorable controversies, Woodcock will also be remembered by those close to the agency for a wide array of work that doesn't typically make headlines – be them good or bad – but was key to a well-run organization.

"One of the things that makes Janet different from most other officials in FDA that I've met, and most other senior people in government that I've dealt with, is she has a very, very strong interest in management. Not just like the sexy policy issues, but how the place runs, how to make it run efficiently, how to make it run fairly, and to create processes that are durable," Sklamberg said.

Woodcock is often credited with "modernizing" the agency's drug division by creating systems, standards and formal processes that allow the center to run somewhat like a machine.

"She more than any person built this giant process, the approval process, the policies and all the things that we take for granted now in how drugs get approved and then ultimately how they get evaluated postmarket," Sklamberg said.

> *"If you need order brought to chaos, call Janet Woodcock," a former colleague said.*

She set up standard operating procedures and an array of formal manuals of policies and procedures known as (MAPPs) so that in many ways the FDA's drugs center will continue to operate consistently even without her at the helm. And she had a strong interest in project management and making sure decisions and policies were properly implemented.

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A lot of senior people in government delegate these types of tasks away because they are boring, Sklamberg said. But Woodcock realized that "you can't just concentrate on … the really interesting approval questions. You have to get into the nitty gritty of making sure the machine works."

"In order to do my job effectively, you have to be willing to empty the bedpans," Woodcock would say, according to Sklamberg.

Woodcock understood she couldn't just do the high-profile glamorous parts of her job for the agency to be successful. "In any employer that has thousands of employees and spends billions of dollars, if you're just out in the public and going to meetings and you're not focusing on the organization that's being run, you're not a good manager," Galson said.

"Dr. Woodcock would be compared favorably to CEOs of major corporations in the way that she has modernized the management of the drug center and of FDA."

She was also extremely accessible, Sklamberg added.

"She was available all the time to solve problems that were, some people would say, below her paygrade. But if it was important, and you needed her input and her judgment, she was always available."

And she was the kind of leader who could remain calm and navigate the agency through crises. "If you need order brought to chaos, call Janet Woodcock," a former colleague said.

Overcoming Sexism

At 73 years old and the height of success, it would be easy to forget that when Woodcock first entered medicine it wasn't a field friendly to female physicians or drug developers.

"I went to med school in the '70s and it was like, 'What, we allow women into med school,'" Woodcock told the *Pink Sheet*. One school she interviewed for said to her "'Well you'll get pregnant and then you just won't be useful as a doctor.'"

Unfortunately, she said, the bias and disparities are still "very striking."

"Even within fairly recent memory, I was at a conference, a small conference of drug developers, there was a picture of all attendees, I was the only woman and there were like 30 other people. And I was the only person who thought, what's wrong with this picture? So it hasn't changed that much."

As to how she managed to thrive and rise to the top of her profession despite those obstacles, Woodcock credited her success to "probably the same thing that's garnered me some critics."

"I just tried to do what I think is right and I don't care what people think. There were some times I was very frustrated because I knew that things that should be done [at FDA] that people ignored me [and] I knew they did it because I was a female. … But I'm a pretty cool individual, I don't let things get to me. I mean, otherwise I couldn't have done this for so long. I'm not that crushed by what other people think," she said. "My focus is on getting things done."