POLITICO

Accelerating drug approvals in the Trump era

A POLITICO Working Group Report.

Big changes could be coming to the way new drugs are approved by the Food and Drug Administration. The Trump administration and incoming new leadership at the FDA, coupled with the implementation of the 21st Century Cures Act, signed into law by President Obama in December, may shake up the status quo for the prescription drug approval process. The Cures Act enables faster drug approvals by expanding the kinds of evidence, beyond traditional clinical trials, that the FDA can consider when reviewing drug applications. For example, the law opens the door to using so-called surrogate markers to evaluate a drug's efficacy; and real- world data are likely to play an increasing role in determining how well drugs work and for whom, or to spot safety problems that may emerge when a drug is used in a broad population. The Trump administration seems to support this direction but uncertainty looms over precisely how the administration will proceed – and what new policies may be introduced or modified as Congress works on renewal of FDA user fees.

What will these changes mean both for patient safety and for the pace of drug approval? What new policy issues do these changes raise? How will the surrogate markers be defined and verified? What does "real-world data" look like in the real world? How will these changes affect coverage decisions by insurance companies? What, if anything,

can the FDA do to pass on any resulting cost savings to patients and taxpayers?

POLITICO recently convened a working group of policymakers and stakeholders to explore the obstacles, risks and opportunities presented by this policy shift. In an on-the-record discussion moderated by POLITICO's executive editor for Health, Joanne Kenen, and health care reporter Sarah Karlin-Smith, the group of specialists and stakeholders identified potential challenges and policy options facing the new administration.

In order to encourage a free and frank conversation, comments were not attributed to individual participants. What follows is their candid assessment of the drive to speed up drug approval while protecting patient safety. The participants are listed at the end of this report.

THE SCOPE OF TRUMP'S CHANGE TO THE FDA

1. Incremental Change Expected

There was broad consensus among the participants that while the drug approval process at the FDA will change under the new administration, the changes will be more incremental than some political rhetoric suggests. The FDA will not be unrecognizable from where it is today by the end of Trump's term in office.

"The change will probably only go as fast as the science in terms of approvals, but I think the opportunities may be few. Probably the largest opportunity is going to be in the next three months, and I'm not sure that the current administration, given the other

things that they're trying to take on will be all that focused on modifying the FDA in the context of the user fee reauthorization."

"In the context of oncology drugs, the change will be incremental, but I have to add, that's because the oncology division has been pretty forward thinking for years, and already has made a number of innovations that have sped drug approval in the last few years, anyway."

"I do think that while you're not going to see big changes, or major new legislation in the upcoming four years, I think you are likely to see some regulatory changes, particularly given the way the commissioner, or looking like who's going to be the commissioner, in the generic drug approval space"

SAFETY AND EFFICACY

The 21st Century Cures Act expands the use of so-called surrogate markers – evidence that a drug is likely to produce a benefit that falls short of a clinical result - and real-world data - evidence compiled once a drug is on the market like data compiled from electronic health records. However, there are risks in relying on data that are not from clinical trials. Participants voiced concern that Congress and the new administration are putting too much emphasis on speeding up approval, and should have more understanding of what the FDA is doing to approve drugs safely and expediently.

"You want it fast? Or you want it right?"

"We have a private system of drug development, so FDA traditionally doesn't test drugs, even though member of Congress don't realize that."

1. Challenge: Surrogate markers do not provide sufficient evidence of drug effectiveness

Although 21st Century Cures expands the use of surrogate markers with the intention of speeding up drug approval, the group cautioned that there are limitations to what these markers can show about whether a drug works. A surrogate has to be scientifically validated – meaning it has to be shown to predict a specific clinical outcome – but many surrogates fail to provide a complete picture of a drug's efficacy. A common example: A drug may be approved because it is shown to shrink a tumor -- but later it's discovered that the drug did not extend patients' lives. Most participants said the FDA should not lean on the surrogate markers presented to them as evidence without strong scientific validation.

"One of the challenges … is the inadequacy of most of the surrogates that are submitted and claimed. And unfortunately, in oncology, most of the surrogates make for big headlines and big p-values in trials, but they don't necessarily translate … a surrogate changes dramatically while the endpoint you really care about, like survival, changes very little."

"We see almost half of all new drug approvals rely exclusively on surrogate markers for their primary endpoints. And when you follow those drugs into the real world, after they're on the market, to see other trials, to see if they're validating those surrogate

markers with clinical endpoints, you just don't see [effectiveness]."

"If the science is good, if you can make the case for a surrogate marker….That's going to come from the research side ... If you want to speed up the FDA review process, fund the NIH budget."

2. Policy Option: Post-Approval Monitoring:

With a new administration that is focused on approving drugs quickly, some participants suggested the FDA should institute enhanced monitoring systems to look out for red flags – either regarding safety or efficacy - after drugs are approved.

"What's the real goal here? Is the goal to maximize safety and then a little bit let the chips fall where they may? Or are you really worried about making 100 percent sure you have an efficacious product before you approve it? ... What I do predict will happen in the coming administration is you will have more of a slant towards the former … I think the important thing there is that you have a robust post-approval surveillance mechanism."

"Everyone should be excited about real-world evidence; it should be faster, it should be cheaper, it can let us look at populations that are broader than our studies and clinical trials. it's just that there's a huge gap now between the reality and the rhetoric. And so there are issues around governance and business models, and progress is being made but it's not mature ... Can you make sense of EHR data? And can you pull data together and actually does it mean what it says"

"What we've heard here talking about real-world evidence, everything is sort of being grouped as the same…and there isn't really anyone on a national level who's adjudicating high quality evidence versus something that is a lower level, and is there a role further down the road for the FDA to be able to do some sort of post-market assessment?"

Several participants noted real-world data can also be used to build evidence for a secondary indication of an approved drug.

3. Challenge: Gaps in data and technology inhibit sharing of real-world data

Participants suggested that a lack of technology and other resources – as well as the need for adequate personnel – inhibit the FDA's ability to use real-world data for drug approval, and later post-market monitoring.

"Medicine lags the rest of the modern economy, in terms of digitalization. And notwithstanding the conversion to electronic medical records systems, the inoperability in a practical sense, not a technical sense, remains profoundly limited and limiting, and we give up a tremendous amount of potential learning because it's either poorly recorded, incompletely recorded, or not sharable in the existing ecosystem."

4. Policy option: Improve Technology and Innovation:

Several participants said a reallocation of resources to the FDA is key to supporting 21st Century Cures' goal to speed drug approval while maintaining safety standards.

“FDA needs to have this innovative tools and staff and resources to relay innovative science and advance science as it’s coming in.”

“Right now, the FDA says yes to a new use, or it remains silent, but for FDA to play an active role in commenting on the level of evidence on a whole bunch of unapproved uses, they need a lot of resources that they don’t have now.”

Outside the FDA, several participants were hopeful that PCOR.NET- the National Patient-Centered Clinical Research Network, which is designed to use patient data to conduct clinical research - would prove to be a useful platform for evaluating the strength of real-world data in a prospective, randomized fashion.

"So if that’s what we’re talking about for real-world evidence, that’s a cheaper trial that can recruit faster and collect data faster. That’s fantastic. But otherwise, it’s observational data, and it has all of the flaws that observational data has always had."

PRICES

Allowing the FDA to approve drugs based on plausible, but incomplete evidence, has prompted insurance companies to reconsider their coverage decisions - whether a health plan will cover a drug, and how much of the cost a patient may bear. Working group participants disagreed on the impact of new approval processes on drug prices.

“The idea that a faster approval process equals lower prices: we have no evidence for that.”

“If you have more drugs on the market, then you have the opportunity … to have a real robust formulary, and drive prices down.”

Several participants voiced concern that pricing on drugs approved with incomplete evidence creates an access problem, particularly if the drug is very expensive.

1. Policy option: value-based payment models

The group considered ways of using the level of evidence behind a drug approval to determine the price of that drug – with the price lower if there’s not strong proven value. Several participants suggested the government and private insurers could work together to create a tiered pricing system to address access problems posed by faster drug approvals. They also noted that paying for drugs based on how well they work would require more research comparing different treatment options against each other.

“Does there need to be more of a role of the government in saying, ‘OK, if we approve the product based on this threshold of evidence, you should start at the lower price, and then maybe as you actually show better evidence, we’ll let you increase the price’”

“The idea is we’re lowering the bar for evidence prior to approval, with the expectation that more evidence will be accumulated after approval, and why not consider staggered prices?”

Some participants questioned the feasibility of adjusting coverage based on updated data, while others noted that this model would be part of a larger trend in health care toward value-based care.

"I still don't totally understand how the insurer just says, 'I'm only going to pay you this much now, because maybe I'll give you more next year, or maybe I'll give you less next year'"

"So, we pay for a value, and we pay incrementally based on whether you're better than something else. But you need the data in order to do that, which is actually more regulation, because then you have to do more clinical trials."

2. Policy option: transparency measures

Some participants said industry would benefit from increased transparency by the FDA about the evidence for a drug's approval. It could mitigate the difficulty insurers will face making payment decisions with incomplete information.

"We have to be careful not to put payers in the position because of FDA regulatory policy, that they don't have the evidence available to them to make the decision on whether or not to cover, and whether or not something has sufficient value for their members."

COST SAVINGS TO PATIENTS AND TAXPAYERS

Participants were divided over whether the approach of the new administration and 21st Century Cures Act would get drugs to market

faster in ways that would yield significant savings for patients, taxpayers and payers.

“The sooner you get to market, the sooner the clock starts ticking, the sooner we get to competition.”

“There needs to be greater collaboration from FDA, what data they will find acceptable for regulatory decision-making … there needs to be stakeholder process when people can come together, discuss what’s appropriate and not, but get real clarity from FDA what it’s going to accept, so company can use it."

But several participants – while lauding the goal of faster access to drugs in the abstract – feared that the push for speed could harm patients in the long run, either by letting unsafe drugs on the market, or by giving patients drugs that just don’t work very well, but that may cost a lot.

Some participants disagreed, saying this approach would accomplish marginal cost savings at best:

“As much as we want to be able to speed up the trial evaluation process, at best we were going to find minor efficiencies. I mean, science is hard. There are lots of failures. You know, there’s a reason most drugs drop between phase one and phase two, and then a lot of the phase twos don’t move on to phase threes, because science takes time, and we find that a lot of them don’t work.”

1. Policy option: Re-evaluating the FDA's role in drug pricing

The FDA does not weigh in on prices, and participants disagreed on what the optimal level of FDA involvement in setting prices should be.

"This idea of faster approval process equals lower prices? We have no evidence for that."

"The FDA is only a very small piece of that answer, and having political rhetoric think that the answer is changing the FDA's current process, that's not going to work."

"I think it actually could be playing a far larger role because it's evidentiary standards, it's incentives motivates the evidence that can be used to set drug pricing, right?"

"There is room to streamline generic prices. A commissioner can do one or two things, and get one or two things done. So, an efficient generic drug approval process, with no backlog, and where companies don't stand in the way with ridiculous arguments and slow down the process, probably is something that is doable."

Working Group Participants:

- Jeff Allen, President and CEO, Friends of Cancer Research
- Margaret Anderson, Executive Director, FasterCures
- Allan Coukell, Senior Director of Health Programs, The Pew Charitable Trusts
- Don Dempsey, Vice President, Policy and Regulatory Affairs, CVS Health (*Sponsor)

- Carol Forster, M.D. Physician Director, Pharmacy and Therapeutics/Medication Safety, Mid-Atlantic Permanente Medical Group
- Tegan Gelfand, Director, Policy and Regulatory Affairs, CVS Health (*Sponsor)
- Paul Howard, Director of Health Policy, the Manhattan Institute
- Clifford Hudis, M.D., CEO, American Society of Clinical Oncology
- David Kessler, M.D., Former Commissioner, FDA
- Lynn Quincy, Director, Health Care Value Hub, Consumers Union
- Martha Rinker, Vice President of Public Policy, National Organization for Rare Disorders
- Joseph Ross, M.D., Associate Professor of Medicine and Public Health, Yale University
- Lucy Vereshchagina, Deputy Vice President, Science and Regulatory Advocacy, PhRMA
- Joel Zinberg, M.D., Visiting Fellow, American Enterprise Institute and Associate Clinical Professor of Surgery at the Mount Sinai Medical Center