FDA approving drugs after fewer trials, providing less information to public, studies find

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The U.S. Food and Drug Administration is approving more novel pharmaceutical drugs based on single clinical trials and with less public

disclosure about those trials than was the norm just a few years ago, a pair of recent studies from Oregon State University has found.

Researchers agree it is important to minimize delays in making treatments for diseases such as cancer available to patients, but they say their findings point to a need for greater transparency around how drugs receive approval.

For many drugs that have been tested in multiple clinical trials, pharmaceutical companies are only required to share the results from two trials, leaving questions about why they chose those two for submission and what happened in the other trials, study co-author Veronica Irvin said.

"We're not saying that cancer drugs need a lot more studies; just that they should show all the results or trials that are completed," said Irvin, an associate professor in OSU'S College of Health. "It doesn't mean they wouldn't get approved, but it means we'd have a more complete picture."

The research team focused on the period after implementation of the federal 21st Century Cures Act, passed with bipartisan support in 2016 and meant to accelerate approval of new medicines so patients could gain access to life-saving drugs that would otherwise take years to become available.

As part of that law, the FDA relaxed some standards to allow treatments for priority health conditions such as cancer to be approved with fewer supporting studies, and placed less emphasis on randomized clinical trials, allowing pharmaceutical companies to rely on surrogate markers instead of clinical outcomes in certain cases. Surrogate markers are used as substitutes when the direct clinical outcomes take a long time to study, and they should be related to the clinical outcomes.

For example, Irvin said, it might take years of following patients in a long-term clinical trial to determine if a drug reduces their risk of a heart attack, so measuring the surrogate marker of blood pressure enables the drug to move through the approval process more quickly. However, reduced blood pressure does not assure reduced risk of death from heart disease, she said.

The studies, published in the *JAMA Network Open* and *Health Affairs Scholar*, reviewed FDA approvals for novel drugs in in 2017 and 2022 to determine how many trials were used to evaluate each drug prior to receiving approval from the FDA.

Researchers also looked at the availability of drug trial results on the public-facing ClinicalTrials.gov, a database maintained by the National Institutes of Health that patients can use to learn more about drugs they may be prescribed.

Of the 37 drugs approved by the FDA in 2022, 24 (about 65%) were approved based on a single study. Four of the 37 drugs (about 11%) reported three or more studies before approval. Roughly half of the 413 studies available for analysis were classified as randomized clinical trials, while results were publicly posted on ClinicalTrials.gov for only 103 of the 413 studies.

In 2016, prior to the Cures Act, only four of 20 novel drugs (20%) were approved based on a single trial.

In the *Health Affairs Scholar* article, researchers found that of the 46 novel drugs approved in 2017, 19 (41%) were approved based on results from a single study—though the drugmakers conducted an average of 2.2 studies per drug, including 165 studies for the popular weight-loss drug Ozempic.

Despite drugmakers completing an average of 5.82 studies per drug prior to FDA approval, results were disclosed on ClinicalTrials.gov prior to approval for only 1.42 studies on average.

That doesn't necessarily mean the FDA is denied access to those full results, Irvin said, but the public cannot read the results until they are posted publicly.

For 33 of the 46 medications (72%), at least one brand-new result was posted on ClinicalTrials.gov within nine months after approval had been given, but in many cases the studies had been completed prior to FDA evaluation.

"Everything is supposed to be transparent with this FDA process," Irvin said. "The purpose of ClinicalTrials.gov was to have a way for the non-scientific community to access the trials and their results, in a way that people can understand."

When the FDA states that it has reviewed drugmakers' two submitted studies, consumers are missing information about how many other studies were conducted, what those results showed and why those specific two studies were chosen for evaluation, Irvin said.

"We want doctors and patients to be able to see the whole picture," she said.

Lead author on both papers was Robert Kaplan from Stanford University, with co-author Amanda Koong, a medical student at the McGovern School of Medicine in Texas.

More information: Robert M Kaplan et al, Food and Drug Administration novel drug decisions in 2017: transparency and disclosure prior to and 5 years following approval, *Health Affairs*

Scholar (2023). DOI: 10.1093/haschl/qxad028

Robert M. Kaplan et al, Review of Evidence Supporting 2022 US Food and Drug Administration Drug Approvals, *JAMA Network Open* (2023). DOI: 10.1001/jamanetworkopen.2023.27650