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New Era Requires New Approach to Drug Approvals

With a coming flood of new drugs to fight COVID-19, a study suggests innovative ways for the FDA to speed up the approval process.

Based on the research of Francisco Polidoro Jr.

During the next year, the Food and Drug Administration will review many new drug applications. Many of them will work in ways regulators haven't seen before, because they're taking on a new and deadly pathogen: the novel coronavirus.

What can the agency do to get ready — especially with public pressure to approve new treatments as quickly as possible?

Francisco Polidoro Jr., associate management professor at Texas McCombs, has a suggestion: Don't look at innovative new drugs through old lenses. Be prepared to design new standards for judging their effectiveness.

In new research covering 35 years of drug applications, Polidoro finds that a major hurdle is the FDA's experience with older drugs. He found that the more information the FDA had about existing drugs, the longer it took to OK new ones for the same conditions.

"Sometimes knowledge can become a hindrance, and too much of a good thing can become a bad thing," he says.

When there was more information about older drugs, more than half the newer drugs in the study took more than 20 months to win approval. By contrast, only 20% of new drugs took that long, when less information was available about older drugs. Although the agency ultimately approves most drug applications, waiting costs their creators an average of $1 million a day.

In the midst of a pandemic, postponing a promising treatment could also cost public health, Polidoro says, as regulators err on the side of caution. "They may avoid making a good therapy available, while they're trying to avoid putting out a therapy that turns out to be bad."

Falling into Regulatory Ruts

Polidoro has long studied organizational routines, processes that preserve knowledge from past experience. In ordinary circumstances, he says, routines

are efficient. A company doesn't have to reinvent hiring rules each time it seeks a new employee, for example.

Organizations can become inefficient, though, when confronted with novel challenges. From minutes of FDA meetings, he suspected that the inertia of old routines might be slowing the approval of innovative drugs.

By "innovative," he means that a drug attacks an illness through a new and different mechanism. In spite of that, regulators often look for the same types of clinical outcomes they've seen from older drugs.

He points to the Alzheimer's drug memantine. Previous drugs had slowed memory decline in early-stage patients. But memantine aimed at later-stage patients. They were already memory-impaired, so the old measures might not be relevant. After lengthy debate, regulators devised new criteria for approval: impact on daily tasks such as dressing and bathing.

> "Regulators search for solutions in the neighborhood of what they already know. They have a harder time when the next big thing emerges." — Francisco Polidoro Jr.

Too Much Information

Do outdated routines hold up the reviews of new drugs? From the FDA, Polidoro got data on 291 medications approved from 1980 to 2014. He divided the drugs into 18 therapeutic classes, from controlling blood pressure to fighting viruses. For each drug, he determined whether it used a mechanism that was new to the class.

To quantify the FDA's knowledge of existing drugs, he counted the number of papers published in top medical journals for each class — an average of 155, sometimes more than 1,000. The more research regulators have on old drugs, he reasoned, the more pressure they would feel to judge new entries by the same yardsticks.

"They feel they have to look for the same outcomes, even when a new drug is working in different ways," Polidoro says.

He found that the more papers existed for a class of drugs, the longer it took for new drugs to win approval. When the measure of papers increased by 32% beyond the average, the result was a 75% longer approval time.

Practice Makes Speed

But there's a way to hasten such approvals, the study finds: practice. The more applications the FDA reviewed for groundbreaking drugs, the faster it got at approving them.

> "As it struggles with innovations, the organization becomes better able to deal with them. It gets more used to breaking routines and creating new ones." — Francisco Polidoro Jr.

That could be good news for fighting COVID-19, he says. Regulators may have to develop several new types of standards, because different drugs attack the illness in different ways. One in clinical trials, tocilizumab, prevents inflammation of lung tissue. Another, remdesivir, blocks the virus from reproducing.

"It will be difficult to compare these solutions with each other because they have different safety and efficacy profiles," Polidoro says. "They're not like apples to apples."

Pharmaceutical companies can help make the FDA's job easier, he adds. They can point out the ways in which new medications differ from old ones. They can suggest new kinds of benchmarks for gauging their success.

After some initial hiccups, Polidoro expects the approval pipeline for COVID-19 treatments to run more smoothly. "In sorting out the differences across different therapies, regulators may become more adept at approving new drugs," he says. "It may be more complicated for them at first, but in the long run, we will all be better off."

"Knowledge, Routines, and Cognitive Effects in Nonmarket Selection Environments: An Examination of the Regulatory Review of Innovations" was published online June 2020 in Strategic Management Journal.

Story by Steve Brooks