Detecting rare blood clots was a win, but US vaccine safety system still has gaps

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The quick detection of an ultra-rare blood clotting reaction in some COVID-19 vaccine recipients showed the power of a federal warning system for vaccine safety issues, but experts worry that blind spots in the

program could hamper detection of other unexpected side effects.

Before the pandemic began, the Food and Drug Administration had scaled back a program it used successfully to track adverse events during and after the 2009 H1N1 influenza pandemic, and the agency is still ramping up its replacement, said Dr. Robert Chen, scientific director of the Brighton Collaboration, a nonprofit global vaccine safety network.

"It's purely bad luck they were in between systems when COVID hit," said Chen, who helped create the existing U.S. vaccine safety systems during nearly 30 years at the Centers for Disease Control and Prevention.

FDA officials acknowledged that some data analysis won't start for weeks or months, but said the government is watching for vaccine reactions with "state-of-the-art" systems.

"FDA and CDC have robust safety and effectiveness surveillance systems in place to monitor COVID-19 vaccines authorized for emergency use in the U.S.," Abby Capobianco, an FDA spokesperson, wrote in an email.

No question, the nation's vaccine surveillance system performed as expected this spring when it identified unusual cases of blood clots combined with low platelet counts in 15 people who had received Johnson & Johnson's one-shot COVID-19 vaccine, said Dr. Jesse Goodman, a former chief scientist with the FDA. Three people died.

"The good news for a very rare event is it will pop up on VAERS," Goodman said on a call with reporters, referring to the Vaccine Adverse Event Reporting System jointly run by the FDA and CDC since 1990.

But other potentially dangerous, unanticipated reactions to vaccines may

not be so obvious in VAERS, a system that is believed to miss many potential side effects—or in the nation's additional monitoring systems, including the Vaccine Safety Datalink and the CDC's new phone-based tracking program, v-safe.

"It's quite a hodgepodge of different systems of collecting data," said Dr. Katherine Yih, a biologist and epidemiologist who specializes in vaccine surveillance at Harvard Pilgrim Health Care. "It's worth stating that it's not as good as it could be."

The Vaccine Safety Datalink, though highly regarded, did not include enough vaccinations within its data from nine hospital systems covering 12 million people to catch the J&J issue, CDC officials said. And enrollment in v-safe has been less than expected, with about 6 million people enrolled by the end of March, just 6.4% of those who had been vaccinated at that point.

That means that, at a time when about 100 million Americans have been fully vaccinated against COVID-19, the U.S. continues to rely on a patchwork network of vaccine monitoring systems that may fail to monitor a large enough swath of the population, experts told KHN.

"I'm very concerned about this," said Goodman, who also led the FDA's Center for Biologics Evaluation and Research, or CBER, and is now a professor of infectious diseases at Georgetown University. "I think we should be seeing that reporting on all of these vaccines. It was promised four months ago that it was happening."

The three vaccines in use in the U.S.—produced by Pfizer, Moderna and Johnson & Johnson—were shown to be safe and effective during clinical trials of tens of thousands of volunteers.

But even the best trials aren't large enough to capture all problems,

especially rare ones, if they occur only in certain groups or outside a specific time frame. It's important to track side effects once vaccines are distributed throughout the population—an effort known as pharmacovigilance—to ensure not only safety, but also public confidence.

Vaccine safety experts said they were concerned that the FDA scaled back a system known as the Post-Licensure Rapid Immunization Safety Monitoring network, or PRISM, long regarded as a workhorse of surveillance.

"Prior to PRISM, I felt like we were sort of in the dark ages," Steve Anderson, director of the FDA's Office of Biostatistics and Epidemiology, said at a 2016 workshop. "When PRISM came along, for us it was really a game changer."

PRISM linked four large health plans in different parts of the country with eight state immunization registries. During the H1N1 pandemic, it detected signals for three adverse events possibly linked to the vaccines and was used to rule out the two that weren't related and the one, Guillain-Barré syndrome, that was.

The system included records from nearly 40 million people, said Daniel Salmon, former director of vaccine safety at the National Vaccine Program Office. Having a large volume of records of vaccinated people "really drives your ability to figure out what's going on," he said.

PRISM, which was repurposed for drug safety, now contains data from about 60 million people, but it has not been used to track vaccine reactions during the COVID-19 pandemic, said Salmon, who oversaw safety monitoring for the H1N1 vaccine.

"With PRISM, we tested it in a crisis and it operated for a decade," he

said. "I was really surprised when it wasn't used for COVID. That was why we built it."

A newer system, called the Biologics Effectiveness and Safety System, or BEST, was started in 2017, but only recently began monitoring data weekly for 15 pre-specified adverse events among Medicare recipients. It will be expanded to include commercial databases starting by the end of June, according to Capobianco, the FDA spokesperson.

A search for possible cases of the rare condition linked to the J&J vaccine began in mid-April and will be expanded in the next few weeks, she added.

FDA officials said PRISM's capabilities have been incorporated into BEST, which can examine data from 100 million people. Experts told KHN that it has not been used extensively to monitor post-vaccination effects, but Capobianco said: "We disagree."

"BEST is built as a state-of-the-art active surveillance system," she wrote.

The concern is that officials have leaned heavily on VAERS, a "passive" system that relies on reports from patients and health care providers to flag issues after vaccination that may or may not be related to the shots. A robust "active" surveillance system can search large volumes of patient care records to compare rates of adverse events in people who received vaccines with those who didn't.

In addition, some vaccine safety experts point to a lack of clear authority in the area. The Trump administration shut down the NVPO, a federal office with expertise in monitoring vaccine safety, merging it into a government agency focused on infectious diseases.

As a result, monitoring of COVID-19 vaccine safety is fragmented among federal agencies, said Salmon, who now directs the Institute for Vaccine Safety at the Johns Hopkins Bloomberg School of Public Health.

"There is no single person in charge," he said. "You need to have somebody in charge."

Biden administration officials have praised the nation's vaccine monitoring system, pointing out that it flagged the Johnson & Johnson problems within weeks of the vaccine's rollout. Federal officials paused distribution to assess additional cases and next steps. (They were helped by the fact that European regulators had found similar problems in another vaccine.)

"VAERS performed exactly as intended in this case," said Dr. Tom Shimabukuro, head of the CDC's COVID-19 Vaccine Task Force.

That's true, said Dr. Steven Black, co-director of the Global Vaccine Data Network. Still, he noted, there's room for improvement, particularly more funding and better collaboration.

"This is a safeguard for our population," Black said. "Whether it's for the flu vaccines or the COVID vaccines, you need to have a viable and strong system. Just because we think they're safe doesn't mean you don't need systems in place to back up that opinion."