Ensuring Safety of a COVID-19 Vaccine via Technology

FDA's post-surveillance methods ensure the continued safety of a vaccine through the collection and monitoring of health data.

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As the Food and Drug Administration prepares for COVID-19 vaccine authorizations and approvals as a result of the Department of Health and Human Services' Operation Warp Speed clinical trials, the agency is also focused on strengthening surveillance efforts on the vaccine's long-term safety.

During FDA’s Vaccines and Related Biological Products Advisory Committee meeting last week, the agency's Center for Biologics Evaluation and Research (CBER) Office of Biostatistics and Epidemiology (OBE) Director Steven Anderson outlined the
agency's plans to monitor COVID-19 vaccine safety and effectiveness in this later phase.

“FDA’s approach for safety is really a ‘safety throughout the lifecycle’ approach for vaccines and regulated products, and that includes pre-licensure as well as post-licensure space,” Anderson said.

He noted two types of post-licensure programs for continuous safety surveillance monitoring: active and passive.

FDA's active risk identification and analysis data systems for monitoring vaccines and other medical products were created as directed by the FDA Amendments Act of 2007 and with funding from the Prescription Drug User Fee Act VI of 2017, Anderson said.

One of these systems is Sentinel, for example. Part of Sentinel is the Biologics Effectiveness and Safety System (BEST).

Unlike passive programs, active surveillance programs can collect adverse event data using automation, such as natural language processing and machine learning. The BEST system collects real-world data from electronic claims data sources — including the claims data of approximately 55 million elderly people ages 65 years and older enrolled in the Centers for Medicare and Medicaid Services. FDA and CMS have been looking at vaccine safety and effectiveness through claims data since 2002, Anderson said.

For its passive surveillance program, CBER OBE has partnered with the Centers for Disease Control and Prevention’s immunization safety office on the Vaccine Adverse Event Reporting System (VAERS), which comprises reports on death and other serious adverse events.

Both agencies meet biweekly to coordinate on the system and pharmacovigilance activities, Anderson said, while OBE’s epidemiology physicians review reports for serious adverse events for COVID-19 vaccines. The teams also employ statistical techniques like data-mining methods within the VAERS system to identify adverse events that are disproportionally or frequently reported, he said.

“What we're looking for in data systems are really rapid data-access for near real-time surveillance, large databases of tens of millions of patients for evaluating rare
serious adverse events, and data representing integrated care spectrum,” Anderson said regarding post-market monitoring data criteria.

“We want high-quality data because it's very important to get,” he continued. “If you identify a safety signal, it's very important to adjudicate that and get that validated properly. You want data with significant clinical details and, preferably, access to medical charts.”

Still, there are limitations in addressing regulatory questions around vaccine safety and effectiveness through claims and EHR data, such as limits in the measured population, timely data reporting, clinical details and the scope of data collected from health settings of interest.

CBER is also looking at rapid-cycle analyses (RCA) surveillance methods to pull potential questions from phase III safety trials for the real-time surveillance and evaluation of post-market COVID-19 vaccines.

The agency has used RCA reliably since 2007 to monitor vaccines for seasonal influenza and Cuillain-Barre Syndrome. With these methods, the agency expects to watch “10 to 20 safety outcomes of interest," though the agency will ultimately support CDC’s RCA for COVID-19 vaccine safety, Anderson said.

CBER will follow studies on the general effectiveness of COVID-19 vaccines for treating subpopulations of interests — like individuals with more than one medical condition and the elderly — as well as how long their protections last.

Additionally, CBER is developing master protocols “both for safety and effectiveness outcomes” regarding COVID-19 vaccine surveillance and their potential adverse effects, in consideration of agency transparency. The protocols will be released as a draft for public comment with the final protocol posted online after the review period.

COVID-19 vaccine safety monitoring efforts will also continue to develop and improve through close coordination with other federal agencies, including CDC, CMS, the Department of Veterans Affairs, the National Institutes of Health, Defense Department and Indian Health Service.
“The idea of sharing plan protocols and discussions on safety and effectiveness outcomes are of joint interest to us,” Anderson said, “and we're coordinating those plans for near real-time surveillance with our sister agencies.”