Mammoth trove of post-market data mined for safety studies

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Physicians likely will recall news reports pertaining to post-market studies on the safety and effectiveness of dabigatran vs. warfarin, as well as the safety of the hypertension medication olmesartan medoxomil.

What those reports had in common was that they came out after the drugs had already won Food and Drug Administration (FDA) approval and had been tracked by the agency's Mini-Sentinel network, which was the five-year pilot program for what was launched as the Sentinel System in 2016. The system now has the capability to answer questions about medical product safety using data from participating health plans and hospital networks.

"The evidence generated by the Sentinel System can provide critical insights to assist health care providers make data-driven decisions about patient care," said Stephen Mikita, FDA patient representative. "The Sentinel System is a powerful safety tool that further protects the public's health."

Mikita is leader of the agency's Sentinel Engagement Partners Workgroup, of which the AMA is an active member.

Created by the 2007 Food and Drug Administration Amendments Act , the Sentinel System electronically monitors FDA-regulated products through the use of a distributed data network. That means the data isn't located in a central repository, but held by 17 participating organizations that maintain ownership of the health information of nearly 300 million people who, between them, generated 13.3 billion unique medical encounters between 2000 and 2017.

Sentinel aims to generate evidence on the use of medical products under real-world conditions. It also helps better characterize unexpected patient reactions and drug interactions to inform FDA regulatory actions. The evidence is disseminated through regulatory and scientific channels to support data-driven clinical care, the FDA says.

Partners in the endeavor include insurance companies, Hospital Corporation of America, and integrated provider networks such as the Marshfield Clinic Research Institute in Wisconsin, Vanderbilt

University Medical Center and six branches of Kaiser Permanente.

“It’s worth noting that Sentinel sites keep their databases locally behind their own firewalls and just send query results off to the coordinating center,” said Robert Greenlee, PhD, a senior research scientist at Marshfield Clinic Research Institute’s Center for Clinical Epidemiology and Population Health.

“At Marshfield, the population we define for Sentinel is predicated in part on membership in our health plan, and so health care claims data play an important role for completeness of capture. But we also incorporate delivery side data from our electronic health record, including lab results.”

On the lookout for the unexpected

Another data partner is health insurer Harvard Pilgrim Health Care, which was awarded the contract to operate the network during its pilot phase. In fall 2014, the FDA awarded Harvard Pilgrim a contract for up to $150 million to lead the Sentinel System.

In January 2017, Sentinel data became available outside the agency through the public-private partnership known as the Innovation in Medical Evidence Development and Surveillance System.

One goal is to develop Sentinel as a national resource for uses such as public health surveillance or clinical decision making.

“We are proud that Sentinel has contributed to the public health mission of the FDA,” said Richard Platt, MD, Sentinel System principal investigator in the Department of Population Medicine at Harvard Medical School and Harvard Pilgrim Healthcare Institute. “The system has enormous potential for future growth, and we look forward to continuously developing the system to help patients everywhere.”

The strengths of the Sentinel System were seen last December, when *Annals of Internal Medicine* published an FDA-funded, retrospective follow-up study to the previous dabigatran vs. warfarin comparisons that were published in 2012, based on data from the Mini-Sentinel network. After identifying more than 971,000 atrial fibrillation patients who had received either drug between November 2010 and May 2014, researchers were able to match 25,289 dabigatran users with 25,289 warfarin users.

Compared with warfarin, dabigatran was associated with a lower rate of intracranial hemorrhage, a similar rate of hospitalized ischemic stroke and “possibly” a higher rate of heart attack, researchers said. They added that these results “give insights to potentially assist in decision making about stroke prevention strategies” for certain patients.

Finding data for clinical decisions

While that discovery didn’t warrant further regulatory action, a safety announcement was issued in 2013 after the Mini-Sentinel network helped uncover how use of the hypertension drug olmesartan medoxomil was associated with intestinal problems. Product labeling was also changed.

Gerald Dal Pan, MD, director of the Office of Surveillance and Epidemiology in the FDA Center for Drug Research and Evaluation, called Sentinel “an important tool in the drug safety toolbox.”

Read more about the Sentinel System and search its reports.