FDA's Sentinel System: Strategies for Expansion and Transformation

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The FDA Sentinel System started as a congressional mandate in the FDA Amendments Act of 2007 and has given rise to one of the world's premier evidence generation platforms. From 2000 to 2019, the distributed database has collected information on more than 300 million patients, including 70 million members who are accruing new data, and beneficiaries of both federal and private insurance. The Sentinel System operates on a distributed database design that enables Sentinel to be one of the largest multi-site, privacy-preserving, medical product safety surveillance systems with highly-curated data in the world. None of this would have been possible without the enormous and essential contributions of our partners to the success of the Sentinel System. Their sharing of data and scientific expertise allowed FDA to fulfill its important public health mission.

2019 marks the success of three full years of the Sentinel System serving as a fully functional and integrated part of the regulatory process at FDA. In a short amount of time, Sentinel has quickly proven to be a vital source of safety information that can inform regulatory decision making and expand our knowledge of how medical products perform once they are used widely in medical practice. FDA has conducted hundreds of analyses in the Sentinel System in a much more efficient manner than was previously possible.

For example, the Sentinel system has provided important information about the utilization of opioids and has contributed to FDA's strategy to intervene to combat this public health crisis. Sentinel System data have also been featured in numerous Advisory Committee meetings, providing important information on the safety of gadolinium-based contrast agents; rates of diabetic ketoacidosis after use of novel anti-diabetic agents; and contextualized results emerging from a post-market cardiovascular clinical trial, just to name a few. FDA has used this evidence in regulatory decision making to contextualize post-market clinical trials and pregnancy registries and inform labelling decisions. FDA has found it feasible to study more than 18 different safety issues that would have otherwise resulted in an industry-required post-market safety study in the Sentinel System.

Testbed for Other Demonstration Products

The FDA Catalyst program is showing how the Sentinel System Infrastructure can also prove useful as a testbed for demonstration projects like IMPACT-Afib, a randomized clinical trial that will determine whether education on stroke prevention in atrial fibrillation (AF) among AF patients and their providers can result in increased use of oral anticoagulants (OAC) for stroke prevention. Such projects create opportunities to develop and evaluate the capabilities for pragmatic trials and mobile applications to collect patient-generated data that were prominently featured in FDA's Real-World Evidence Framework released earlier this year.

In the Sentinel System, FDA has also launched projects to evaluate how advanced analytics such as Natural Language Processing (NLP) and Machine Learning (ML) can address gaps when human expert-constructed algorithms based on coded data cannot fully meet the needs. This is especially important when data are available but hard to standardize, as is the case for laboratory, radiology, and pathology results that are sometimes needed to confirm a diagnosis. FDA has launched several

new projects to leverage Electronic Health Records (EHRs) to address these problems, targeting the outcomes of anaphylaxis, acute pancreatitis, and rhabdomyolysis. FDA recently initiated a collaboration with the People Centered Research Foundation (PCRF), the successor to PCORnet, the largest network of electronic health record data in the US. FDA will test and evaluate how this new data source might contribute to the mission at FDA. FDA's push to leverage advanced data analytics, acquire deeper data sources such as EHRs, and expand our core scientific capabilities is described at length in the Sentinel Strategic Plan published in January 2019.

FDA is also guided by a broader vision to create a national resource for evidence development. This vision encompasses FDA's Real World Evidence programs and safety surveillance activities, but extends beyond the evaluation of medical product safety and efficacy, into biomedical science, quality improvement, and the learning healthcare system. FDA has made substantial progress toward fulfilling this goal for the Sentinel System to become a national resource for evidence development and a cornerstone of a learning healthcare system. The Initiative's partner organizations now use their data, methods, and tools to work with the Reagan-Udall Foundation Innovation in Medical Evidence Development and Surveillance program, the National Institutes of Health Care Systems Research Collaboratory Distributed Research Network, the Patient-Centered Outcomes Research Institute's PCORnet, and the Biologics and Biosimilars Collective Intelligence Consortium.

Sentinel's tools and data structures have also been used by manufacturers of products regulated by the FDA, and they have been adopted by the Canadian Network for Observational Drug Effect Studies program, enabling regulatory agencies to execute a single query in both national systems. Additional opportunities exist for leveraging the FDA investment in the Sentinel System, including broadening engagement with the public health community to support chronic and infectious disease surveillance activities by federal, state, and local public health agencies. Opportunities also exist for supporting new quality improvement programs for delivery systems and payer organizations.