EVENT SUMMARY

Forum on Post-Market Evidence
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ENGELBERG CENTER for Health Care Reform
at BROOKINGS

Overview of Recent FDA Drug Safety Activities

The Food and Drug Administration Amendments Act (FDAAA), enacted last year, calls on the FDA to establish an active surveillance system to identify additional risks associated with medical products already on the market. This "Sentinel" system will use large sets of electronic health care data from a variety of sources to detect signals related to adverse events. FDAAA requires that the Sentinel system be operational on 25 million lives by July 1, 2010.

The FDA's current system for discovering adverse events is based on spontaneous reports. This will remain an important part of the agency's work even after the Sentinel network becomes operational. The FDA also participates in other safety-surveillance initiatives, like the Vaccine Adverse Events Reporting System and the Observational Medical Outcomes Partnership, which test methods for using and assessing observational data.

Building a National Network for Drug Safety

To guarantee that the Sentinel initiative is a success, the FDA and other public and private stakeholders must address several inter-related challenges. Building the system will require development of a governance process and sophisticated infrastructure. Also, in order to effectively utilize the system, researchers need to develop new methods for signal detection and validation within the network. Finally, a strategy is required for communicating Sentinel objectives and findings to the public in a timely, transparent, and credible way.

Key Challenges and Possible Solutions

Infrastructure and Governance
The Sentinel system could be constructed as a distributed data network – a system where individual patient data remains with data owners and behind system firewalls and researchers can only see summary-level data in response to system queries. In this way, data generally stay with those government agencies, payers, or providers who know the data best and are already charged with maintaining its privacy and security. The capacity for "traceback" for case confirmation was also discussed.

Reflecting the consortium nature of Sentinel activities, which draws on a range of public and private data sources and expertise, it has been proposed that the system be coordinated by a public-private partnership such as the Reagan-Udall Foundation, a non-profit organization created by the FDAAA. An executive board composed of representatives from a variety of stakeholder groups would craft procedures on the use and management of the Sentinel infrastructure, and the FDA would act as the ultimate decision-making authority on Sentinel governance issues. A scientific advisory committee will help create and enforce policies to ensure that studies conducted using Sentinel system data are methodologically sound.

Although the FDA and others have put forward a potential governance structure for the Sentinel network consistent with this framework, many organizational process questions have yet to be answered. For instance, policies regarding network access, network funding, and intellectual property rights have not been firmly established.

Data and Methods Issues
Some level of standardization across "data environments" will be necessary so that the same queries and programs can be run across the distributed data network. Ideally, all databases would have an audit trail capability, tracking information on who used the data and how the data was used. Effective signal detection will also require the development of new statistical methods to analyze data and validate query results.

Many methodological issues still require further development. Among other things, researchers will need to determine the minimum set of data elements needed for robust analyses, how to consistently analyze exposure and outcomes in the distributed data environment, and how to interpret the collective set of results generated by the network on any given research question. In the short run, researchers will need to identify best practices from existing methods; over time, researchers will need to create new methods for analyses in distributed data environments. These efforts will require additional funding and collaborative research initiatives. Fortunately, the Sentinel initiative creates a unique opportunity to create a new scientific "social network." These interactions—across settings and disciplines—could stimulate new breakthroughs driven by the new, large-scale data analysis opportunities. Sentinel partners need to ensure that experts from a wide range of fields are attracted to the developing field of safety surveillance research.

Legal and Privacy
The law firm Coppersmith Gordon Schermer & Brockelman conducted an analysis of the legal issues surrounding a drug safety surveillance program. Their analysis concluded that the legal risks associated with such a project are not prohibitively high, as long as adequate attention is paid to privacy and security issues. At the federal level, the Health Insurance Portability and Accountability Act's (HIPAA) Privacy Rule allows the use of individual health information for both public health activities and research. The analysis concluded that the FDA's involvement is crucial because HIPAA (and many state laws) explicitly permit disclosure of health information to the agency or its designees for the purpose of post-marketing surveillance. The analysis also concluded that a drug safety surveillance program structured as a research protocol will comply with federal privacy laws, as well as those of most states.

If the Sentinel initiative is defined as a research project, it must conform to privacy regulations detailed in the Federal Policy for the Protection of Human Subjects. This policy, known as the "Common Rule," usually calls for Institutional Review Board (IRB) oversight of research in order to ensure that research subject privacy is protected. To ensure that the Sentinel initiative has an efficient review process, it may be useful for the initiative to utilize a central or multi-center IRB.

Finally, FDA reporting requirements will shape Sentinel initiative activities. When the Sentinel system detects a safety signal, the pharmaceutical company that manufactures the drug associated with that signal must determine the nature of the relationship between the drug and the signal. If there is an acute, causal relationship between the drug and the detected adverse event, the pharmaceutical company must produce reports for the FDA. The company must also notify physicians of any newly discovered drug risks.

Communications and Impact on Practice
The communications strategy must establish and maintain the credibility of the Sentinel system. If the network lacks credibility, safety signals may simply be disregarded by the public. Sentinel-related communications must balance the need to inform the public about possible risks in a timely manner with the possibility of reporting false signals. Also, patient privacy concerns create another high-priority communications issue. In order to assuage worries about privacy, partners in the Sentinel initiative need to make sure that the public understands how the Sentinel network will use health care data.

Sentinel partners should promote public discussion about treatment risks and benefits. Too often, consumers assume that the FDA's approval of a treatment implies the treatment is "zero risk." Consumers should understand that safety actually means an acceptable risk given the level of benefit in the context of the population affected and the available alternatives.

Finally, health care providers will also need to be informed about the Sentinel system, how it works, and how study results should be interpreted.

Next Steps

The Engelberg Center for Health Care Reform at Brookings is committed to the development and public dissemination of solutions to the challenges raised at this conference. Over the coming months, the Engelberg Center will continue to bring together stakeholders and experts to provide guidance, , and will conduct further analysis on the topics of Sentinel governance and infrastructure, data and methods, legal and privacy issues, and communications.

Existing programs – such as the Vaccine Safety Datalink, eHealth Initiative's Connecting Communities for Drug Safety, and the HMO Research Network – demonstrate the potential for operationalizing Sentinel. The Engelberg Center at Brookings will work with leaders of these projects to ensure that best practices are incorporated into future discussions about safety surveillance.