

**Brookings Active Surveillance Implementation Council**

In cooperation with the U.S. Food and Drug Administration (FDA), the Engelberg Center for Health Care Reform at Brookings convened senior public and private sector leaders to discuss appropriate and meaningful ways to engage medical product developers in FDA's post-market surveillance activities, including the Sentinel System. This document highlights the major topics discussed during the meeting.

**Background**

Under contract with FDA, Harvard Pilgrim Health Care Institute, in collaboration with over 20 other organizations, is leading the development of Mini-Sentinel, a pilot system to provide FDA the ability to conduct rapid medical product safety surveillance. Mini-Sentinel is intended to inform the establishment of FDA's full Sentinel System. After a year and a half of infrastructure and methods development, Mini-Sentinel began conducting safety evaluations earlier this year on selected products as requested by FDA. These initial evaluations will not only inform the structure and development of the system, but their findings will also contribute evidence about the performance of these products in the postmarket environment. As a result, medical product developers have expressed an interest in being more involved in these activities. Specifically, they are interested in understanding the results of Mini-Sentinel evaluations as well as FDA's plans for incorporating those results into their regulatory decision-making. Developers are also interested in contributing their product-specific and pharmacoepidemiologic expertise to inform development the system. As the system continues to develop, many expressed their opinion that there is a clear need to involve and clarify the role of medical product developers.

**Taking Advantage of Developer Experience while Maintaining Public Trust**

Because developers are intimately familiar with their products and employ knowledgeable scientists highly trained in pharmacovigilance and pharmacoepidemiology, FDA's Sentinel System could be strengthened by engaging developers in a variety of activities. However, their involvement may also introduce conflicts of interest. To maintain the integrity of the system and preserve confidence in Sentinel's findings, it is essential to find the appropriate context and mechanisms for engaging developers.

Open and transparent communications from FDA to the public addressing topics such as the meaning of a safety signal, steps involved in the surveillance process, steps taken to verify associations that emerge from Sentinel's signal refinement evaluations, and when and how developers engage with FDA throughout those steps can help to address potential conflict of interest concerns and maintain public

accountability. Further, involving a wide variety of stakeholders, including data and analytic partners (D&APs), providers, other federal agencies, and consumer, provider, and patient groups in some of these activities can also mitigate concerns.

### **Specific Areas for Developer Engagement**

Developers are interested in participating in several aspects of FDA's safety surveillance activities, including protocol development, interpretation of results, and methods research and development. Developers have their own pharmacovigilance departments, which cultivate this expertise in parallel with product development. As developers are among the most knowledgeable about their specific products, they would like to provide input into the development of surveillance protocols. Although developers may also wish to be involved in FDA's discussion and interpretation of results, they indicated that FDA should take the helm in all decision-making and communication regarding methods selection and results interpretation; as FDA has a number of other systems in place to monitor drug safety and inform regulatory decisions (e.g., the adverse event reporting system), and the Agency plans to consider Sentinel findings within this broader context. In addition, developers thought it was key to be publicly transparent about any contribution and collaboration between FDA and developers, and also to be inclusive of other stakeholder groups.

Since announcement of FDA's Sentinel Initiative, developers have been engaged in methods research and development through initiatives such as the Observational Medical Outcomes Partnership (OMOP), a public-private partnership that identifies and evaluates appropriate methods and databases for conducting drug safety surveillance. Although OMOP has made significant contributions to surveillance methods, gaps still exist that highlight the need for more work in this area. Developers can continue to support methods research and development by increased participation in OMOP and similar initiatives.

### **Future Initiatives for a Broader Evidence Development System**

The Mini-Sentinel pilot has demonstrated the utility of a distributed data infrastructure for drug and vaccine surveillance. Opportunity exists to build upon this infrastructure to create a broader network of D&APs that can be used for additional evidence development activities (e.g., patient-centered outcomes research, biomedical research, quality of care evaluations) by multiple stakeholders. This broader evidence development system can effectively be organized in the form of a public-private partnership that involves a diverse set of stakeholders including D&APs, federal agencies, developers, academics, patient and providers, and others. Broadening this system will require support for several types of activities that build upon the work that has already been done in safety surveillance, including the development and promotion of data standards, protocols for quality assurance, methods research and development, and standardized definitions for health outcomes of interest. An open-access research lab can also provide training opportunities for young scientists to learn core principles and effective strategies for conducting observational research using data collected for other purposes.

Unlike Sentinel, governance of this broader system should be independent of FDA, although FDA should play an appropriate part along with other public and private sector stakeholders. Effective governance

will require policies that address access to the system, patient privacy, communicating findings, funding, and sustainability, among other issues.

Creating a successful and sustainable public-private partnership for a broader evidence development system will require a clear and compelling business model for stakeholders. Identifying the ways each stakeholder group would benefit from joining the public-private partnership may help to ensure good initial participation. One potential model for access to the system relies on users paying fees or contributing in-kind expertise intended to support ongoing maintenance and necessary improvements to the system.

### **Next Steps**

This meeting outlined the importance of and considerations for medical product developer participation in FDA's Sentinel Initiative and in a potential broader evidence development system. More discussion will be required to elaborate upon the roles that developers can play, particularly in protocol development, methods research and development, and models to ensure sustainability of the system. The Engelberg Center for Health Care Reform will convene a small expert workshop in Fall 2011 with chief medical officers and heads of pharmacovigilance from a number of medical product development companies to further explore technical and strategic considerations regarding their involvement in Sentinel and related evidence development efforts.