ENGELBERG CENTER for
Health Care Reform
at BROOKINGS

March 1, 2012

Discussion Guide

Expert Workshop: Patient and Consumer Engagement in FDA's Sentinel Initiative

Patients and consumers routinely encounter a variety of medical products, including drugs, biologics, vaccines, devices, diagnostic tests, and other products, during interactions with the health care system. At the time of approval, a medical product has been shown to have benefits that outweigh the potential risks. However, throughout the lifecycle of a medical product, the data about its performance accumulates and new information regarding the performance and safety profile of a medical product is learned. For instance, drugs approved based on clinical trial data have been tested in a relatively small and carefully selected population of patients when compared to the general population of patients who may use the drug after it is marketed. Small clinical trials are unlikely to detect rare adverse events associated with use of a drug (e.g., adverse events that occur in one individual for every 100,000 patients who take the drug)—these rare safety concerns are more likely to be detected when a drug is used in a broader population after approval.

Recognizing that many important safety concerns may arise in the post-market environment (i.e., after approval for marketing), the U.S Food and Drug Administration (FDA) routinely reviews multiple data sources to evaluate medical product safety, including reports submitted to the Adverse Event Reporting System (AERS), relevant medical literature, and post-market safety studies. However, post-market safety data collected through these vehicles often accumulate slowly, and the ability to identify actual safety concerns may only emerge after products have been on the market for an extended period of time.

With passage of the Food and Drug Administration Amendments Act of 2007 (FDAAA), Congress mandated that FDA develop a new system to more rapidly identify and understand potential safety issues using very large existing electronic health databases. In response to this charge, FDA launched the Sentinel Initiative to develop a new tool for active medical product safety surveillance that will augment, but not replace, FDA's existing postmarket safety assessment tools. The Sentinel Initiative is composed of four major activities, which are described below.

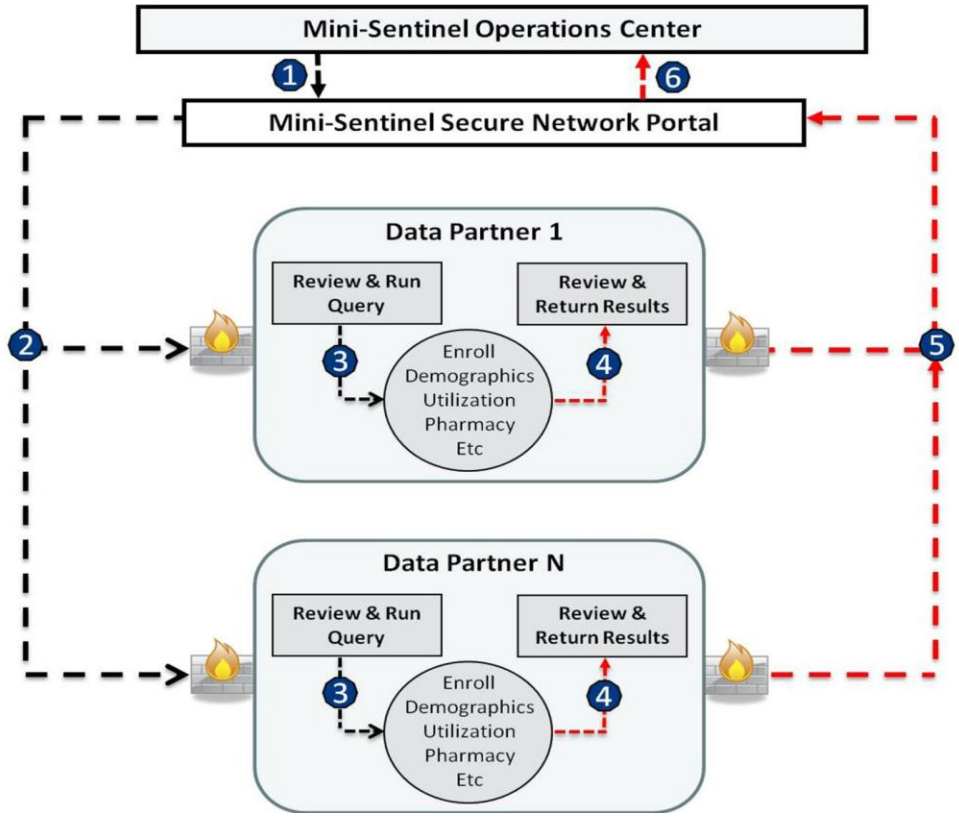
Mini-Sentinel Pilot Project

This pilot project, contracted to Harvard Pilgrim Health Care Institute in 2009, represents a broad collaboration among FDA, academic and private organizations, and scientists (Mini-Sentinel Collaborators) with the goal of developing the infrastructure, methods, governance, and other capabilities necessary for the Sentinel System to conduct active medical product safety surveillance.

A hallmark of Mini-Sentinel is the establishment of a distributed data network for querying health care data. This network consists of the Mini-Sentinel coordinating center and various data partners—private health plans and integrated health systems—that maintain physical and operational control over their patient-level data, which includes electronic health care data such as data from health insurance claims and electronic health records. All activities and analysis of medical data are conducted in compliance with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule. The HIPAA Privacy Rule establishes national standards to protect individuals' medical records and other protected health information and applies to a number of sectors of the health care system, including health plans. The rule requires appropriate safeguards to protect the privacy of protected health information and sets limits and conditions on the uses and disclosures that may be made of such information without patient authorization.

When a question arises from FDA regarding a potential association between a medical product and an adverse patient outcome, the Mini-Sentinel coordinating center (in collaboration with FDA, academic researchers, and other partners) develops and issues a query to each of the data partners in the network. This query takes a question (e.g., Is the rate of myocardial infarction higher in patients taking drug X?) and translates it into analytic code that each data partner can use to run a statistical analysis of its data. To ensure that different sites execute queries from the Mini-Sentinel coordinating center in a consistent manner, participating data partners format their data according to a common format known as the common data model. Each data partner returns only aggregated, de-identified results to the Mini-Sentinel coordinating center. In contrast to a centralized model in which data from each partner are physically compiled and stored in a common warehouse, the distributed data network provides important security and patient privacy protections by keeping data behind data partner firewalls. The distributed approach also takes advantage of data partner expertise, which can help ensure proper use and interpretation of the data.

Figure 1: The Mini-Sentinel Distributed Data Network[1]



1. A query (executable program) is created and then posted to the Mini-Sentinel Secure Network Portal.
2. Data partners are notified and retrieve the query.
3. Data partners review the query and execute it against their local data.
4. Data partners review the results.
5. Data partners submit their results using the secure portal.
6. The results are reviewed and then combined with other data partners' results.

[1] Source: Mini-Sentinel

FDAAA mandated a series of goals for Sentinel, including the ability to query electronic health care data from 100 million people by July 2012. As of December 2011, Mini-Sentinel had already surpassed this goal and could query administrative claims data (e.g., prescription claims data, diagnosis codes, and procedure codes) from over 126 million individuals, more than a third of the U.S. population.

The Mini-Sentinel pilot is focused on signal refinement—refining an understanding of potential safety concerns that have been identified through FDA's other channels. Mini-Sentinel has developed a variety of options for evaluating these suspected safety signals, including rapid assessments that yield basic results within a few days or weeks and more in-depth assessments, which require the development of a customized protocol and therefore take more time to return results. Mini-Sentinel has recently completed rapid assessments of the potential association between angiotensin receptor blockers and celiac disease and drugs for smoking cessation and cardiac outcomes. In 2011, Mini-Sentinel also initiated in-depth assessments to explore the relationship between oral hypoglycemic agents and myocardial infarction and the relationship between the rotavirus vaccine and intussusception.

Consisting of membership from FDA, participating organizations and institutions, and a member of the patient community, the Mini-Sentinel Planning Board is the oversight body of the Mini-Sentinel Pilot. Mini-Sentinel's policies and procedures govern the protection of patient privacy, data integrity and security, confidentiality, and conflicts of interest and intellectual property. Information regarding activities completed by Mini-Sentinel is made available to the public on the Mini-Sentinel website (www.mini-sentinel.org).

Observational Medical Outcomes Partnership
Managed and funded through the Foundation for the National Institutes of Health with contributions from pharmaceutical companies and in-kind donations, the Observational Medical Outcomes Partnership (OMOP) is a public-private partnership established to inform the appropriate use of observational health care databases for studying the effects of drugs. OMOP's specific aims in supporting this goal are to conduct research to evaluate the ability of various methods to identify true medical product-health outcome associations; develop tools and capabilities for transforming, characterizing, and analyzing disparate data sources across the health care delivery spectrum; and establish a shared resource so that the broader research community can collaboratively advance the field of safety science.

Federal Partners Collaboration
This pilot has established a distributed system to conduct safety assessments among several federal agencies and departments, including the Centers for Medicare & Medicaid Services, the Department of Veterans Affairs, and the Department of Defense. Rather than using a common data model and uniform queries, participating agencies and departments work together to develop a shared assessment plan, which is translated to suit the nature and format of each partner's data. Since initiation of this pilot, the Federal Partners Collaboration has developed an understanding of the differences in data characteristics and an infrastructure that allows the agencies and departments to work within their unique data and analytic frameworks.

Brookings' Convening Activities
Under a cooperative agreement with FDA, the Engelberg Center for Health Care Reform at the Brookings Institution convenes a number of meetings to engage stakeholders in both technical and policy discussions related to active surveillance of medical products and the Sentinel Initiative. These meetings bring together the expertise of diverse stakeholders to inform development of Sentinel and are an important vehicle for communicating updates on the Sentinel Initiative to the public. Brookings convenes four types of meetings:

1. Annual public workshops serve as a forum to provide updates on the progress of the Sentinel Initiative and engage the public in dialogue about the direction of the Initiative. These workshops are held at the beginning of each year and are open to the public.

2. Roundtable webinars feature initiatives related to developing methods, data sources, and technology relevant to active medical product surveillance. These hour-long webinars are held approximately every other month, free, and open to the public. Recent webinar topics include highlights from the 2012 Sentinel Initiative Public Workshop and an overview of the active surveillance activities conducted by the Department of Veterans Affairs.
3. Implementation council meetings convene senior leaders from public and private organizations to discuss strategic issues related to the development of a national system for post-market medical product safety surveillance.
4. Expert workshops, such as this meeting, explore a range of issues that will inform development of the Sentinel System. Each meeting brings together a set of content experts specific to the discussion topic. Previous expert workshops have explored biostatistical and epidemiological issues in active medical product surveillance, communicated findings from active medical product surveillance, and set priorities to advance the development of active surveillance methods.

Workshop Objectives

Over the past few years, the Sentinel Initiative has made important strides toward developing a valuable tool for harnessing the potential of electronic health care data to evaluate post-market safety of medical products. As described above, in collaboration with major private payers, academic institutions, scientists and others, Mini-Sentinel has developed and begun to exercise its capability to conduct both rapid evaluations of suspected safety signals and more in-depth and targeted prospective safety assessments. Mini-Sentinel and OMOP have also provided critical new insights into the most accurate and appropriate methods for use in a distributed post-market safety system. These successes were enabled by a productive and broad collaboration among stakeholders from both public and private institutions. At each step of the planning and implementation process, various stakeholder groups have been involved in shaping the approaches adopted and tested by Mini-Sentinel. The future success of the initiative depends on continued collaboration and transparency regarding Sentinel's capabilities and findings.

Patient and consumer organizations have provided an essential perspective and valuable input into Sentinel to date. Since the initiation of the Sentinel Initiative, patient and consumer groups have provided feedback through forums such as the Brookings' annual public workshop and roundtable webinars. In addition, patient and consumer representatives have actively participated in a number of more targeted planning forums, including Brookings' implementation council meetings and expert workshops and the Mini-Sentinel Planning Board and the OMOP Executive Board. Because Mini-Sentinel has started to conduct active surveillance assessments, it will be important to discuss how to evolve and expand upon the involvement of patients and consumers in Sentinel.

This expert workshop aims to engage representatives from a variety of patient and consumer advocacy organizations and the FDA in a dialogue about the ways in which patients and consumers are already involved in Sentinel and opportunities for furthering their engagement. The objectives of this discussion are the following:

- Provide patient and consumer advocates with an overview of the Sentinel Initiative;
- Discuss opportunities for further patient and consumer engagement; and
- Discuss concrete next steps for evolving patient and consumer engagement.

Facilitating Patient and Consumer Engagement

Discussions from previous Brookings meetings have suggested some possible ways to engage patients and consumers in the Sentinel Initiative. These suggestions include the following:

- *Providing guidance on patient and consumer informational needs*: FDA has indicated that maximizing transparency is an important aspect of the Sentinel Initiative. As part of this effort, findings from Mini-Sentinel assessments are being made publically available. However, it is important to recognize

that Mini-Sentinel's findings do not provide definitive answers. The coordinating center distributes queries—requests for data—and each of the data partners return information, which must then be interpreted in the context of a larger body of evidence, such as pre-market and post-market clinical trial data and AERS reports. Some degree of uncertainty is inherent in Sentinel's assessments. Thus, developing effective strategies to communicate Sentinel's findings, capabilities, and limitations to patients and consumers will be important. Input regarding development of these strategies, including what information consumers and patients would like to know about Sentinel and its assessments and how they would prefer to receive this information, is needed now.

- *Providing input into strategies to maintain public confidence in the Sentinel Initiative:* Sentinel's success will also hinge on strong stakeholder and public confidence in the initiative. Some of the steps that Mini-Sentinel is taking to bolster and preserve such confidence include maintaining high data quality, using rigorous active surveillance methods to minimize uncertainty in results, ensuring that results are interpreted appropriately, and avoiding the influence of conflicts of interest by participating organizations and researchers. Patients and consumers could potentially provide further input into additional strategies for maintaining public confidence in Sentinel.

These topics are proposed in the interest of promoting discussion but are not meant to capture the entire spectrum of ways that patients and consumers may be engaged in Sentinel. During the morning session, patient and consumer representatives are encouraged to consider these and other ways through which they could provide meaningful input into the Sentinel Initiative.

The afternoon session will focus on ways to advance and realize ideas discussed in the morning. This may include prioritizing suggestions, developing next steps for advancing these suggestions, and outlining stakeholder roles in this process. Ideas proposed at this meeting will lay the foundation for future efforts to further patient and consumer engagement in the Sentinel Initiative.