ENGELBERG CENTER for Health Care Reform at BROOKINGS

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# DISCUSSION GUIDE

## Expert Workshop: Communicating Findings from Active Medical Product Surveillance

**Background**

Data from premarket development programs and relevant medical literature are available to evaluate medical product safety prior to marketing. Once products are approved and on the market, additional data sources become available, including reports submitted to the U.S. Food and Drug Administration's (FDA) Adverse Events Reporting System (AERS) and postmarket safety studies. However, postmarket safety data collected through these vehicles often accumulate slowly, and safety signals 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 the Agency develop a new system to more rapidly identify potential safety issues using existing electronic health data. In response to this charge, FDA is developing the Sentinel System as a new tool for active medical product surveillance that will augment, but not replace, the Agency's existing postmarket safety assessment process.

In 2009, FDA awarded Harvard Pilgrim Health Care Institute a contract to develop Mini-Sentinel, a pilot that will inform the development of the Sentinel System and create a coordinating center capable of querying automated health care data utilizing a distributed approach. Mini-Sentinel is comprised of approximately 200 investigators including all Vaccine Safety Datalink principal investigators (PIs), 12 AHRQ CERTs PIs, 9 AHRQ DEcIDE center PIs, 12 current/former FDA advisory committee members, 3 IOM "Future of Drug Safety" committee members, 4 International Society of Pharmacoepidemiology presidents, and Critical Path Institute leadership. Mini-Sentinel's data partners include HealthCore, the HMO Research Network, Kaiser Permanente's Center for Effectiveness and Safety Research, Humana-Miami Health Services Research Center, and Vanderbilt. Initially Mini-Sentinel will focus on conducting signal refinement, a stage in the active surveillance process that begins with a potential association between a medical product and an adverse health outcome of interest (HOI) that has emerged from available data. Two general signal refinement scenarios can be envisioned:

- Concern about a specific medical product-HOI pair emerges during the product's development program OR there is a desire at the time of marketing to monitor a product for an association with an HOI that tends to be medical product-related but is too rare to be observed reliably in a development program (e.g., acute liver failure, Guillain-Barre syndrome). In these cases, FDA would want to monitor the potential association at a regular interval over time as the product is taken up into the market.
- Concern about a specific medical product-HOI pair emerges well after the introduction of the medical product to the market. In this case, a one-time retrospective evaluation may be conducted to assess the potential association using the entire extent of marketing history.

The types of analyses conducted during signal refinement may include but are not limited to approximate rates of exposures and outcomes, crude associations, adjusted associations, and evaluations of coherence. To enable timely responses to potential safety concerns, the signal refinement process must proceed as rapidly as possible. The first phase of the signal refinement process involves attempts to establish the rate of exposure in the population and defining the characteristics of the exposed population. Subsequent signal refinement analyses may be more sophisticated, including controlling for confounding variables and risk modifiers. In 2010, Mini-Sentinel developed the infrastructure and tools required to conduct signal refinement. They will begin using those tools in early 2011.

**Unique Challenges for Communicating Findings from Active Medical Product Surveillance**

Active medical product surveillance within Mini-Sentinel will evaluate signals of potential safety issues with specific medical products using a range of epidemiologic approaches. Numerous issues make communicating active surveillance findings challenging. For example:

- Active surveillance findings are just one of many sources of information that may inform regulatory decisions.
- The automated databases used in active surveillance have important limitations.
- Methodological limitations and residual uncertainty around results can make the interpretation of active surveillance findings complex.
- A substantial body of research on risk communication and risk perception suggests that health care providers and patients alike frequently misinterpret risk information due to a limited understanding of quantitative information, numeracy issues, and "warning fatigue."
- Health plans and other organizations participating in active surveillance may feel a "duty to warn" their patients if a safety signal is detected.

Pilot surveillance activities conducted through Mini-Sentinel present an opportunity to address some of these challenging communication issues. This pilot work – coupled with focused dialogue among consumer and patient advocates, health care provider groups, payers, product sponsors, FDA, and safety science experts to discuss the content, timing, and approach to communicating findings from active medical product surveillance – will ensure that the Sentinel System's communications strategies are thoughtful, transparent, responsible, and effective.

**Workshop Objectives and Format**

Discussion during the workshop will focus on the perspective of all stakeholders regarding what, when, and how information from active medical product safety surveillance, such as that being piloted through Mini-Sentinel, should be communicated. The objectives of the meeting are to (1) reach common understanding of current statutory provisions and FDA activities regarding safety and risk communication; (2) discuss stakeholder perspectives and the impact those perspectives could have on active surveillance communication strategies; (3) propose ideas for rapid communication that don't preempt journal publication of more complete analyses; and (4) propose ideas for educating patients, physicians, and other decision makers on how to interpret and apply results from active surveillance.

Each panel will begin with opening comments that are intended to lay out some of the key issues for discussion. These remarks are intended to serve as a primer for subsequent discussion with the larger group of experts in attendance. The questions below will guide the discussion. Workshop participants are encouraged to consider their own perspectives on these issues and come prepared to discuss them.

**Stakeholder Panel I: Patient, Consumer, and Health Care Provider Perspectives**

- At what point will the public, patients, and health care providers want information derived from active surveillance to be communicated to them?
- How can the residual uncertainty associated with active surveillance findings be best communicated?
- From your perspective, what are the unique concerns related to communicating findings from active surveillance, and how can these be addressed?

**Stakeholder Panel II: Sponsor, Data Partner, and Payer Perspectives**

- At what point should information derived from active surveillance be communicated to sponsors, data partners, and payers? Does this timing differ from when it should be communicated to providers and patients?
- What other issues or challenges should be anticipated in communicating findings from active surveillance, and how can they be addressed? For example:
    - What concerns do data partners participating in active surveillance have about the implications of transparency in communicating findings?
    - How might active surveillance-based communications impact formulary placement and reimbursement?
    - How should the findings be placed in the appropriate treatment context?
- What strategies can be used to mitigate these concerns?

**Stakeholder Panel III: Scientist and Publisher Perspectives**

- What can safety scientists and publishers do to ensure active surveillance findings are interpreted and communicated effectively?
- How can safety scientists and publishers help prepare health care providers and other stakeholders to receive and interpret the findings of active surveillance?
- What strategies could be deployed to balance FDA's need for early and open communication with the public with ensuring validity of the results and that ultimately drug safety information is communicated responsibly?