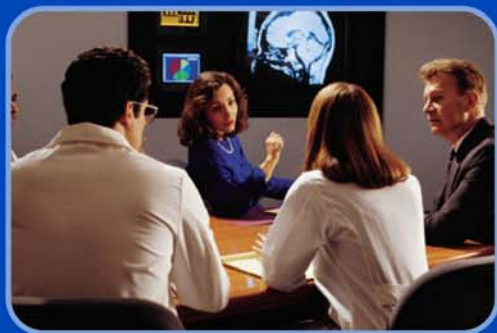


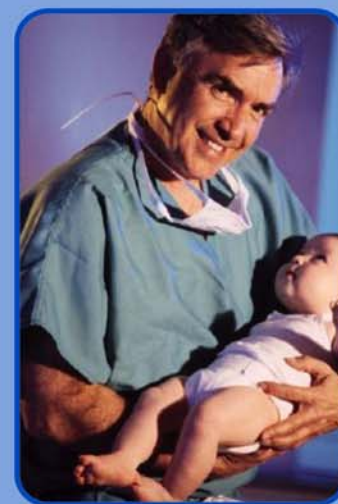
July 2010



The Sentinel Initiative

Access to Electronic Healthcare Data for More Than 25 Million Lives
Achieving FDAAA Section 905 Goal One

An update on FDA's progress in building a national electronic system for monitoring the postmarket safety of FDA-approved drugs and other medical products



U.S. Department of Health and Human Services
U.S. Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy



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EXECUTIVE SUMMARY

In May 2008, the U.S. Department of Health and Human Services (HHS) and the U.S. Food and Drug Administration (FDA) announced the launch of FDA's *Sentinel Initiative*, a long-term program designed to build and implement a national electronic system for monitoring the safety of FDA-approved drugs and other medical products. Once completed, the system under development by the Sentinel Initiative will be called the *Sentinel System*.

The announcement of the Sentinel Initiative followed passage of the Food and Drug Administration Amendments Act (FDAAA), which became law in September 2007. Section 905 of FDAAA mandates FDA to develop an enhanced ability to monitor the safety of drugs *after these products reach the market*. Using a scientific approach called "active surveillance," the Sentinel Initiative is designed to ensure that the Sentinel System will fulfill the mandates included in FDAAA.

FDAAA set goals that FDA's new safety monitoring system must be able to access data from 25 million people by July 2010 and 100 million people by July 2012.¹ FDA met the July 2010 goal for access to patients' electronic healthcare data and is already working towards the patient data access goal of 100 million patients by 2012. Having met the initial goal, FDA recognizes this achievement as an opportunity to provide an update to our progress in building the Sentinel System.

The Sentinel System will enable FDA to monitor the safety of drugs and other medical products with the assistance of a wide array of collaborating institutions throughout the United States. Data partners in the Sentinel System will include organizations such as academic medical centers, healthcare systems, and health insurance companies.

The electronic data used in this process will be accessed, maintained, and protected by the Sentinel System's data partners, as part of a "distributed system." In a distributed system, data remain in their existing secure environments, rather than being consolidated into one database. In addition to data partners, other collaborators involved in this public-private partnership will include, but are not limited to, patient and healthcare professional advocacy groups, academic institutions, and regulated industry.

Within this distributed system, a Coordinating Center will receive and process FDA-generated safety questions. The Coordinating Center, with the collaborating data partners, will develop analytical programs so each data partner can evaluate the questions using their own local computer systems and provide HIPAA-compliant² summary information regarding the questions back to the Coordinating Center and FDA.

¹ (Section 905(a) (3) (B) (i) – (ii) (II)).

² HIPAA refers to the Health Insurance Portability and Accountability Act, which includes restrictions on the use of healthcare data to ensure patient privacy.

The Sentinel System will *augment*, but not replace FDA’s existing postmarket safety monitoring systems. For many years, various parts of FDA have gathered risk information about drugs and other medical products through programs that rely on external sources (such as product manufacturers, consumers, patients, and healthcare professionals) to report suspected medical product-related adverse reactions. This type of safety monitoring is known as “passive surveillance.” In contrast, the Sentinel System will be an “active surveillance” system, so called because it will enable the Agency to initiate its own safety evaluations that use available electronic healthcare data to investigate the safety of medical products.

This *combination of both active and passive safety surveillance systems* will provide FDA a more comprehensive means of monitoring drug and other medical product safety in the United States.

With access to information provided from this broad array of healthcare data partners, the Sentinel System is being designed to enable FDA to obtain vital information to help shorten the time it takes to better understand new or emerging medical product safety issues. This “near real-time” capability is envisioned to help identify safety issues associated with drugs and other medical products earlier in a product’s lifecycle compared to the use of current systems.

Because the Sentinel Initiative is a complex endeavor, FDA has launched several projects designed to help develop the eventual Sentinel System, including two pilot initiatives: *Mini-Sentinel* and the *Federal Partners’ Collaboration*.

- Mini-Sentinel is an effort to develop a smaller working model of the distributed system that is envisioned for the Sentinel System.
- The Federal Partners’ Collaboration leverages the scientific capabilities of other federal government agencies, including the Veterans Health Administration at the Department of Veterans Affairs (VA), the Department of Defense (DoD), and the Centers for Medicare & Medicaid Services (CMS), with the intent to use these federally-held data sources to develop the scientific methodologies needed for active surveillance.

FDA has long envisioned the ability to add “active surveillance” to its wide array of tools to help ensure the safety and efficacy of the medical products it regulates, and was pleased that FDAAA legislation facilitated the launch of these efforts.

FDA strongly believes the Sentinel System will enhance the understanding of medical product safety well into the 21st Century and become a national resource of value for many future generations of Americans.

The Sentinel Initiative: A Progress Report

With the launch of the Sentinel Initiative in May 2008, FDA highlighted in broad strokes its vision of the Sentinel System.³

This 2010 report provides an updated vision of the Sentinel System based on FDA's activities over the past two years, and a description of progress since its launch.

I. SENTINEL SYSTEM VISION

A. Active surveillance via a distributed system

The Sentinel System, as currently envisioned, will enable FDA staff to actively request information from Sentinel System data partners when a safety question arises about a medical product. This scientific approach is known as *active surveillance*. Data partners will include organizations such as academic medical centers and healthcare systems with electronic health record systems, and health insurance companies with administrative claims data.

In the active surveillance environment of the Sentinel System, FDA will prioritize safety questions that have emerged from premarket or postmarket safety data sources (e.g., clinical trial data, spontaneous adverse event reports) and submit them to a Coordinating Center for evaluation by data partners that are part of Sentinel's "distributed system." Within this distributed system, Sentinel System data partners will securely access their databases to evaluate the submitted question and return HIPAA-compliant result summaries to the Coordinating Center. Through data checking and review activities, the Coordinating Center will assess the validity of the results, and then aggregate and forward them to FDA for their use in assessing the safety question.

This information, together with the other benefit and risk information known about a medical product from its premarket development program and other postmarket safety data sources, will enable FDA to enhance its understanding of a postmarket safety issue and inform regulatory decisions and healthcare decision-making, to help protect patients from harm.

B. Sentinel will expand FDA's current safety surveillance capabilities

The active surveillance vision of the Sentinel Initiative complements the largely *passive surveillance* safety systems currently in use by FDA. These passive surveillance systems include the Agency's Center for Drug Evaluation and Research's (CDER's) Adverse Event Reporting System (AERS), a database that captures reports of suspected adverse drug reactions and

³ The *Sentinel Report, National Strategy for Monitoring Medical Product Safety* is available at <http://www.fda.gov/downloads/Safety/FDAsSentinelInitiative/UCM124701.pdf>.

medication errors, FDA's Center for Biologics Evaluation and Research's (CBER's) Vaccine Adverse Event Reporting System (VAERS), a database that captures reports of suspected vaccine-related adverse reactions, and FDA's Center for Devices and Radiological Health's (CDRH's) Manufacturer and User Facility Device Experience (MAUDE) that captures reports of suspected medical device related adverse reactions. In addition to mandatory reporting by industry, FDA receives reports submitted through FDA's MedWatch program, which enables healthcare professionals and consumers (i.e., patients, family members, caregivers) to voluntarily report suspected adverse drug reactions and medication errors.

These spontaneous reporting systems are categorized as "passive surveillance" systems because they must wait for industry, consumers, patients, and healthcare professionals to recognize and report suspected adverse events for FDA to become aware of potential medical product related problems.

Unlike passive surveillance, Sentinel's active surveillance system will enable the FDA to use existing electronic healthcare data in near real-time, a key advantage to more quickly evaluating and understanding a safety issue. Additional advantages of an active surveillance system include the ability of FDA staff to evaluate safety issues in targeted subgroups of patients (e.g., the elderly) and also to have the capability to evaluate adverse events occurring commonly in the general population (e.g., myocardial infarction, fracture) that tend not to get reported to FDA through its passive reporting systems.

II. PROGRESS BUILDING THE SENTINEL SYSTEM

In anticipation of the Sentinel Initiative launch in May 2008, FDA had already begun working with the public and private sectors to establish goals, identify concerns, and initiate activities and pilot programs to lay the ground work for building an active surveillance system for medical product safety. An Attachment to the 2008 *Sentinel Initiative Report* lists dozens of initiatives that were in progress in 2008 in the public and private sectors.⁴ Those collaborations have continued and new ones have been initiated. Two critical pilot programs that are shaping the development of the Sentinel System are the *Mini-Sentinel* pilot and the *Federal Partners' Collaboration*.

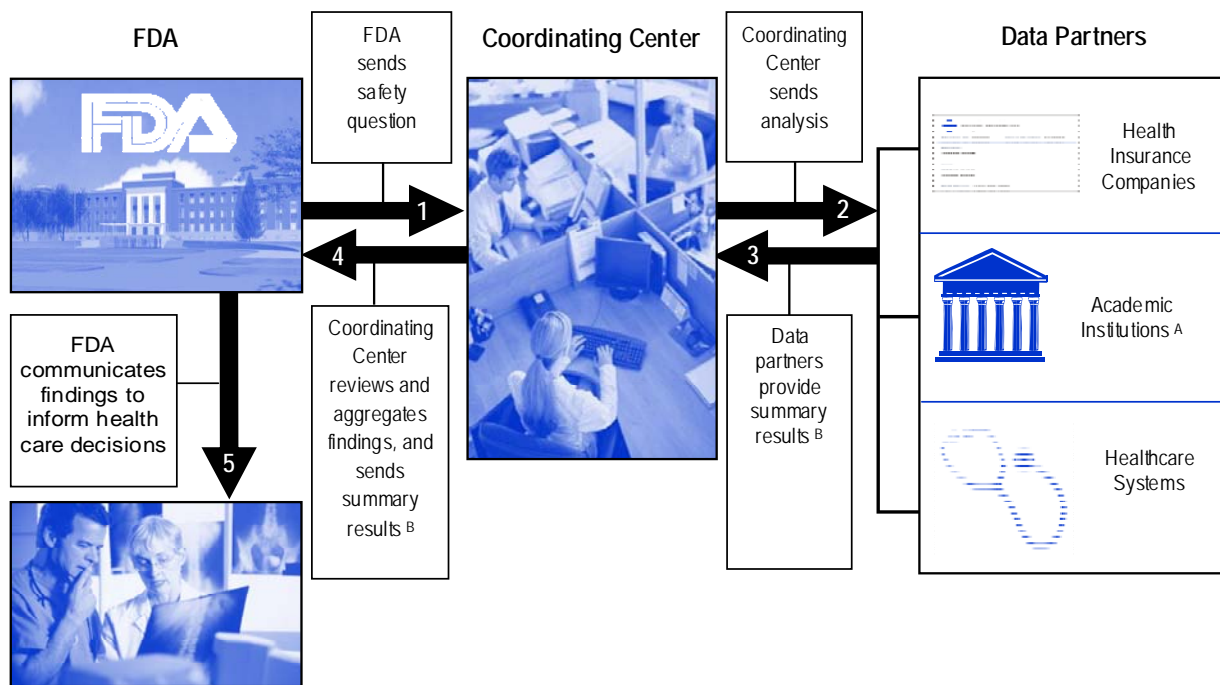
- *Mini-Sentinel*, launched at the end of 2009, will enable FDA to query privately-held electronic healthcare data (including administrative claims and clinical data) representing approximately 60 million patients.
- The *Federal Partners' Collaboration*, which includes the Centers for Medicare & Medicaid Services (CMS), the Veterans Health Administration at the Department of Veterans Affairs (VA), and the Department of Defense (DoD), will enable FDA to query federally-held electronic healthcare data, including administrative and claims data, and data from electronic health record systems.

⁴ The *Sentinel Report, National Strategy for Monitoring Medical Product Safety* is available at <http://www.fda.gov/downloads/Safety/FDAsSentinelInitiative/UCM124701.pdf>.

A. Creating a pilot Sentinel System (Mini-Sentinel)

In September 2009, FDA awarded a contract to Harvard Pilgrim Health Care, Inc. (Harvard Pilgrim) to develop a smaller working version of the future Sentinel System. The pilot has been dubbed “Mini-Sentinel.” Harvard Pilgrim is establishing the Mini-Sentinel Coordinating Center (MSCC) that will operate as a scaled down version of the Sentinel System and enable the Agency to test scientific methods and develop new activities to help create the Sentinel System. The MSCC will lead a consortium of more than 20 collaborating institutions.⁵ As described in Figure 1 below, the MSCC will be able to take FDA-identified safety questions and submit them to participating data partners for evaluation. Data partners will evaluate the safety questions in their database, behind established firewalls, and return HIPAA-compliant summaries of results to the MSCC.

Figure 1: Overview of the Mini-Sentinel Safety Question Evaluation Process



- A. Only those academic institutions with electronic healthcare data will receive safety questions for evaluation.
- B. Data partners will provide summary results from analyses conducted within their secure data environments. Those summary results will not include directly identifiable health information.

⁵ The collaborating institutions in the consortium include the following organizations: CIGNA Healthcare; Cincinnati Children’s Hospital Medical Center; Brigham and Women’s Hospital; Duke University School of Medicine; HMO Research Network sites (includes Group Health Cooperative, Harvard Pilgrim Health Care Institute, HealthPartners, Henry Ford, Lovelace Clinic Foundation, Marshfield Clinic Research Foundation, Meyers Primary Care Institute (Fallon)); HealthCore; Humana-Miami Health Services Research Center; Kaiser Permanente (includes: KPNC, KPSC, KPCO, KPNW, KPG, KPHI, KPOhio, KPmidatlantic); Outcome Sciences, Inc.; University of Illinois at Chicago; University of Iowa, College of Public Health; University of Pennsylvania School of Medicine; Vanderbilt University School of Medicine; Weill Cornell Medical College.

The *Mini-Sentinel* pilot will create a kind of laboratory, giving FDA the opportunity to test epidemiological and statistical methodologies in the evaluation of postmarket safety issues and learn more about some of the barriers and challenges, both internal and external, to establishing a Sentinel System for medical product safety monitoring.

The MSCC and participating data partners will use a common data model as the basis for their analytic approach. The approach requires the data partners to transform their data into a standardized format. Data converted to the standardized format are included as a part of the Mini-Sentinel Distributed Database. Utilizing this standardized data format, the MSCC is able to write a single analytical software program for a given safety question and provide it to each of the data partners. This allows for each data partner to run the program on its standardized data.

Data partners will conduct analyses behind their existing, secure firewalls and send HIPAA-compliant summary results to the MSCC for aggregation and further evaluation.

The MSCC results evaluation process will include checking of the data and analytic program to ensure it ran correctly. MSCC will conduct additional analyses of the results to assess their validity and provide FDA with both the aggregated results and the summary results from each data partner. The use of a common analytic program will minimize the potential for differences in results across data holders resulting from differences in the implementation of an active surveillance protocol.

As part of its contract, Harvard Pilgrim is responsible for ensuring that data use complies with HIPAA. FDA will not require patient-, provider-, or health plan-specific identifiers. Any results provided to FDA will either be aggregated from all data partners or presented as summary results from individual data partners, and supplied in a standard predetermined format. As currently envisioned, all analyses of data will be performed by the data partners in their secure environments without transfer of directly identifiable information.

B. The Federal Partners' Collaboration: Leveraging CMS, DoD, and VA data

FDA is furthering the science of medical product safety surveillance by broadening existing pilot programs that use federally-held data sources. The effort, known as the Federal Partners' Collaboration (FPC), which involves the Federal Partners CMS, VA, and DoD, expands the SafeRx project, a collaboration between FDA and CMS that utilizes Medicare and Medicaid data for medical product safety surveillance. The FPC is similar to the Mini-Sentinel pilot in that it utilizes an active surveillance approach and involves a distributed system. However, unlike Mini-Sentinel, the FPC does not use a common data model. Rather, the FPC develops a common active surveillance protocol, and then each data partner writes analytic code to run the protocol in their database.

Lessons learned from this pilot will be compared to lessons learned using a common data model where centralized analytics are employed (e.g., Mini-Sentinel). In this way, FDA can compare the potential benefits and drawbacks of every data partner running a single analytic program based on a common data model versus each data partner developing its own analytic program based on a common protocol.

C. Achieving the 25 million lives milestone

FDAAA set goals that FDA's new active safety monitoring system must be able to access data from 25 million people by July 2010 and 100 million people by July 2012. Although the Sentinel System is still under development, FDA has established partnerships with multiple data partners that would enable access to healthcare information for more than 60 million lives. Those sources include information from the Federal Partners' Collaboration, including CMS, VA, and DoD, and the data partners comprising the current Mini-Sentinel Distributed Database.

III. PROGRESS ENSURING SECURITY AND PRIVACY

Safeguarding the privacy and security of all information FDA processes is of paramount concern to the Agency. It is a fundamental part of FDA's ongoing responsibilities as it fulfills its mission to protect public health. Since the launch of the Sentinel Initiative, FDA has engaged thought leaders in the privacy and security field. One of the first contracts awarded under the Sentinel Initiative involved the identification and analysis of potential privacy issues.

A. Inherent protections of a distributed system

Within the Sentinel System's distributed system, directly identifiable data will not be transferred to FDA. Instead, directly identifiable data will remain under the local control of participating data partners, behind existing firewalls, and protected by established privacy and security safeguards. Those data partners who participate in the Sentinel System will perform analyses of their own data upon request and provide HIPAA-compliant summary results.

B. Focus on "minimum necessary"

FDA recognizes that there may be infrequent occurrences when de-identified data may not be sufficient for medical product surveillance. There may be instances that require the sharing of more specific information between data partners and the Coordinating Center. For example, in some cases, individual medical record review is required to confirm that a patient had an adverse event of interest. Therefore, FDA is actively exploring approaches that will ensure that only the minimum amount of directly identifiable information necessary leaves its local environment to meet the needs of the specific active surveillance evaluations. FDA is also engaging with privacy experts to explore other avenues of consumer protection that should be developed or expanded.

C. Federal law requires maintenance of system security

The Sentinel System, like all systems that process, publish, transmit, or store FDA information or information on behalf of FDA, must be protected in accordance with the Federal Information Security Management Act (FISMA) of 2002. The Sentinel System must be fully assessed as part of the FDA Certification and Accreditation process as required by FISMA and the Office of Management and Budget before being put into production.

D. Releasing data and findings to the public

FDA has in place a number of mechanisms for communicating safety information to the public, including product labeling and a range of safety communications that are posted on FDA's Web site and disseminated through FDA's MedWatch program. The Agency will follow similarly transparent methods of publicly communicating relevant and timely safety information obtained through Sentinel System evaluations.

IV. CONCLUSION

FDA welcomes this opportunity to report the status of the Sentinel Initiative. We have made significant progress and are committed to continuing this ambitious pace. Attachment 1 shows the many milestones FDA has already achieved in developing the Sentinel System. The requirements laid out by Congress in section 905 of FDAAA will be met and even exceeded. Attachment 2 highlights contracts and cooperative agreements instrumental in the development of the Sentinel Initiative.

Since the launch of the Sentinel Initiative in May 2008, FDA has built upon the work that had already been initiated to expand the Agency's postmarket safety monitoring capabilities to include active surveillance approaches.

Over the coming years, lessons learned from efforts such as Mini-Sentinel and the Federal Partners' Collaboration, will allow us to further refine plans for the implementation of the Sentinel System. These pilots, along with other ongoing activities, will enable us to design the Sentinel System in a way that addresses the complex needs of an active surveillance system, including technological, methodological, legal, and operational challenges.

Importantly, FDA is working to ensure that the privacy and security of directly identifiable information are strictly maintained in accordance with federal and state laws and regulations.

As FDA develops the Sentinel System as a tool to conduct active surveillance on the medical products it regulates, we are careful not to lose sight of its potential value to other public and private entities. FDA envisions that the Sentinel System will become part of a larger national partnership that will meet the needs of regulators as well as others including healthcare systems, academicians, and the regulated industry. Such a partnership would be of interest, not only to those evaluating the safety of medical products, but also to those aiming to improve the quality of healthcare.

We are working to ensure that the Sentinel System's distributed system of electronic healthcare data is developed in such a way that it becomes a national resource of value for future generations, providing the maximal value to the public health.

ATTACHMENT 1. SENTINEL INITIATIVE MILESTONES

Sept. 2007	Congress passes FDA Amendments Act (FDAAA) requiring FDA to collaborate with federal, academic and private entities to develop methods to obtain access to disparate data sources and validated means to link and analyze safety data. FDAAA establishes goals of including 25,000,000 patients by July 1, 2010; and at least 100,000,000 patients by July 1, 2012.
March – Sept 2008	Sentinel Team kicks off its series of Stakeholder meetings, including meetings with other Federal agencies and outside stakeholders (patients, consumers, academics and other experts, potential data partners, vendors, regulated industry).
May 2008	FDA launches Sentinel Initiative and issues a report outlining the program and its goals.
June 2008	Sentinel Team establishes Federal Partners Working Group, which meets quarterly to explore issues related to the Sentinel Initiative and other related federal initiatives.
Aug-Sept. 2008	Sentinel Team awards eight contracts to inform the Agency on the development of the Sentinel System by addressing issues related to governance, privacy, data and infrastructure, scientific operations, and outreach (see Attachment 2).
December 2008	Sentinel Team and eHealth Initiative Foundation cosponsor the public workshop <i>Sentinel Initiative: Structure, Function and Scope</i> , in cooperation with Brookings Institution. Stakeholders participating include academia, potential data partners, vendors, consumers, patient representatives, Federal partners and industry.
Sept 2009	Sentinel Team awards a cooperative agreement to The Brookings Institution to convene discussions on topics related to active medical product surveillance.
Sept 2009	Sentinel Team awards two contracts to inform the Agency on the development of the Sentinel System addressing issues related to privacy regulations at the state level and data sources for veterinary medicine safety surveillance (see Attachment 2).
Sept 2009	Sentinel Team awards a contract to Harvard Pilgrim Health Care, Inc. to create a Coordinating Center to support the development of the scientific operations for the Sentinel Initiative (“Mini-Sentinel”).
Jan 2010	2 nd Annual Sentinel Initiative Public Workshop is convened by the Brookings Institution’s Engelberg Center for Health Care Reform and supported by a grant from the FDA.
Jul 2010	FDA access to 25 million patients achieves a FDAAA mandate.

ATTACHMENT 2. CONTRACTS AND COOPERATIVE AGREEMENTS TO INFORM THE AGENCY ON THE DEVELOPMENT OF THE FDA SENTINEL SYSTEM

The following documents are now available in the FDA docket and on the Sentinel Web site <http://www.fda.gov/Safety/FDAsSentinelInitiative/default.htm>.

- *Developing a Governance and Operations Structure for the Sentinel Initiative*, an eHealth Initiative Foundation report.
- *Engagement of Patients, Consumers and Healthcare Professionals in the Sentinel Initiative*, an eHealth Initiative Foundation report.
- *Defining and Evaluating Possible Database Models*, a Harvard Pilgrim Health Care, Inc. report.
- *Evaluation of Existing Methods for Safety Signal Identification*, a Group Health Cooperative Center for Healthcare Studies report.
- *Evaluation of Potential Data Sources for a National Network of Orthopedic Device Implant Registries*, an Outcome Sciences, Inc. report.
- *Evaluation of Timeliness of Medical Update for Surveillance in Health Care Databases- and IMS Government Solutions* report.
- *Evaluating Potential Network Data Sources for Blood and Tissue Product Safety Surveillance and Studies*, a Pragmatic Data report.
- *Evaluation of State Privacy Regulations and Relation to the Sentinel Initiative*, a Qual-Rx report.

Work on the following projects is still ongoing.

- *Evaluation of Potential Data Sources*, a Booz Allen Hamilton report.
- *Evaluation of Potential Data Sources for Animal Drugs used in Veterinary medicine*, an Insight Policy Research, Inc. report.
- *Detection and Analysis of Adverse Events to Regulated Products in Automated Healthcare Data: Efforts to Develop the Sentinel Initiative*, Harvard Pilgrim Health Care, Inc.
- *Convener of Active Medical Product Surveillance Discussions*, The Brookings Institution.