Report to Congress

The Sentinel Initiative — A National Strategy for Monitoring Medical Product Safety

Department of Health and Human Services
Food and Drug Administration

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Commissioner of Food and Drugs

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EXECUTIVE SUMMARY

The Food and Drug Administration Amendments Act of 2007 (FDAAA)[1] required the Food and Drug Administration (FDA) to collaborate with public, academic, and private entities to develop methods for obtaining access to disparate data sources and to validate means of linking and analyzing safety data from multiple sources.[2] Additionally, FDAAA set goals that FDA be able to access data from 25 million patients by July 2010 and from 100 million patients by July 2012.[3]

In light of this mandate and as a result of several years' planning, in May 2008, the Secretary of Health and Human Services (HHS) and FDA's Commissioner announced the ***Sentinel Initiative***, a long-term effort to create a national electronic system for monitoring FDA-regulated medical product safety. The *Sentinel System*, which is being developed and implemented in stages, will ultimately expand FDA's existing postmarket safety surveillance systems by enabling FDA to actively gather information about the safety and performance of its regulated medical products once they reach the market.

FDA is pleased to report that significant progress has been made on the overall Sentinel Initiative, and the agency is committed to continuing this ambitious pace during the coming years. Even prior to the launch of the Sentinel Initiative in May 2008, FDA had begun actively implementing this effort through scientific and technical activities and through discussions with the public. With the 2008 launch, FDA was able to expand its efforts to create a broad public forum to gather additional input on the perspectives and concerns of all stakeholders in the healthcare community and expand and initiate new activities.

A key finding from the early work of the Sentinel Initiative is that a distributed data system is the preferred approach for organizing the active surveillance system. A distributed system will allow data to be maintained in local environments by current owners, as opposed to using a centralized approach, which would consolidate the data into one physical location. A key benefit of the distributed approach is enabling the maintenance of patient privacy by keeping directly identifiable patient information behind local firewalls in its existing protected environment. Additionally, each health care data system has unique characteristics, and use of a distributed system better enables the data owner's involvement in running analyses to ensure an informed approach to interpreting results.

Summary of Achievements

Meeting Congressional Goals: The specific data access goals put forth by Congress in Section 905 of FDAAA are being met; the 2010 goal was exceeded in July 2010.

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[1] Public Law 110-85.
[2] Section 905
[3] Federal Food, Drug, and Cosmetic Act, Section 505(k)(B)(i)–(ii)(II), added by Public Law 110-85, Section 905(a) (3).

Progress in System Design/Development: Building on experience and knowledge gathered from several small contracts, two active surveillance pilot projects have been launched: *Mini-Sentinel* (through a private-sector contract) and the *Federal Partners Collaboration.*

- The *Mini-Sentinel pilot* is giving FDA the opportunity to develop the data infrastructure and scientific operations needed to conduct active safety surveillance of medical products within a distributed system. Mini-Sentinel's coordinating center is based at Harvard Pilgrim Health Care Institute; 26 collaborating institutions contribute data, methods expertise, or both (see www.mini-sentinel.org). Mini-Sentinel has also incorporated the Post-Licensure Rapid Immunization Safety Monitoring (PRISM) program into its operations. PRISM was launched by HHS in collaboration with FDA and the Centers for Disease Control and Prevention (CDC) for H1N1 vaccine surveillance.
- The *Federal Partners Collaboration* (FPC) is an extension of *SafeRx*, which was a collaboration between FDA and the Centers for Medicare & Medicaid Services (CMS) with initial funding support from the HHS Assistant Secretary for Planning and Evaluation and which was expanded to include the Departments of Veterans Affairs and Defense. The FPC is giving FDA the opportunity to work with its Federal partners within a small distributed system to investigate shared medical product safety concerns.

This ongoing work is creating the framework for designing and developing the eventual Sentinel System. Through these pilots, FDA is leveraging the power of large private and public health care databases to enhance the understanding of medical product safety profiles. FDA is working with participating organizations to test a distributed model for data access and analytical tools for active safety surveillance of medical products.

Guaranteeing Privacy and Security: Concerns raised by numerous stakeholders, including how to guarantee the privacy and security of personally identifiable information, are being carefully addressed. One of the initial tasks of the Mini-Sentinel pilot was to consider how best to ensure compliance with laws and regulations related to privacy and protection of electronic healthcare data being used for medical product surveillance.

Maintaining Transparency: Since the official launch of the Sentinel Initiative in 2008, FDA has worked very hard to create an environment that facilitates transparency in every way possible and involves extensive public and private participation.

Developing a National Resource: Developing and implementing the Sentinel System is a long-term, scientifically and technologically very complex undertaking. As FDA works with stakeholders to create the Sentinel System as a tool to conduct active surveillance on the medical products it regulates, we must not lose sight of the potential value of the infrastructure it helps create to other public and private entities. FDA believes that the Sentinel System should be developed in a way that creates a ***national resource*** for both the Federal and private sectors, providing maximal value to the broad public health. We envision the Sentinel System to become part of a large national infrastructure that supports regulatory responsibilities, but also facilitates the work of academicians and regulated industry.

The Sentinel Initiative is providing an opportunity for the broad medical and scientific communities to partner in the establishment of a significant foundation for future research. FDA is enabling the collaboration needed to make this vision a reality through its outreach to other government agencies and the private sector, with the goal of achieving economies of scale, reducing duplication of efforts, and leveraging available human and financial resources. This type of collaboration is critical.

Throughout this effort, FDA has been extremely vigilant to ensure that the Sentinel Initiative progresses in the most transparent way possible with extensive public and private participation. The Initiative cannot succeed without the full participation of the healthcare community.

Report to Congress

The Sentinel Initiative — A National Strategy for Monitoring Medical Product Safety

I. BACKGROUND

Section 905(c) of the Food and Drug Administration Amendments Action (FDAAA) of 2007, [4] provides the following reporting requirements for FDA:

> *Not later than 4 years after the date of the enactment of this Act, the Secretary shall report to the Congress on the ways in which the Secretary has used the active postmarket risk identification and analysis system described in paragraphs (3) and (4) of section 505(k) of the Federal Food, Drug, and Cosmetic Act, as added by subsection (a), to identify specific drug safety signals and to better understand the outcomes associated with drugs marketed in the United States.*

Section 905 of FDAAA specifically called for the HHS Secretary to develop methods to obtain access to disparate data sources and to establish a postmarket risk identification and analysis system to link and analyze health care data from multiple sources. The law set goals of accessing data from 25 million patients by July 1, 2010, and from 100 million patients by July 1, 2012. The law also required FDA to work closely with partners from public, academic, and private entities.

In May 2008, the Secretary of HHS and FDA's Commissioner announced the Sentinel Initiative,[5] a long-term effort to create and implement a national electronic system for monitoring FDA-regulated product safety. The Sentinel System is intended to augment FDA's existing postmarket safety surveillance systems by enabling FDA to actively gather information about the postmarket safety and performance of its regulated products.

What is the Current Vision for Sentinel?

The Sentinel System, as currently envisioned, will serve as an *active surveillance system* to monitor the safety of marketed medical products. Sentinel will employ a *distributed system*, in which personally identifiable information would remain with its data holders in its local environment, protected by existing firewalls and managed by those most familiar with the data.

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[4] Food and Drug Administration Amendments Act of 2007, Public Law 110-85, was signed into law in September 2007. See Title IX, Section 905.

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

Across the scope of medical product safety surveillance, we envision three categories of activities: signal generation, signal refinement, and signal evaluation. A *safety signal* is a concern about an excess of adverse events compared to what is expected to be associated with a product's use.[6] Safety signals may be generated from a variety of sources including the product's clinical development program, postmarket studies of a product, or postmarket adverse event reports submitted to FDA's spontaneous reporting systems. Additionally, statistical methods can be applied to healthcare data (either spontaneous reports or administrative claims data) to identify outliers that may represent safety signals.

In an effort to minimize the likelihood of identifying false positive safety signals, FDA is initially focusing its efforts on signal refinement. Within signal refinement, FDA further evaluates a safety signal for which there is already some evidence of a concern, either based on data from the clinical development program, postmarket studies or adverse event reports, or due to a theoretical safety concern related to the type of medical product or the class that the medical product is in. Should a signal refinement assessment provide additional evidence supporting the safety signal, additional work may be done to confirm the signal. Recently, FDA has also begun exploring ways to improve signal generation methods to further develop active surveillance capabilities.

In Sentinel's current active surveillance pilots (see Section II), we have chosen a distributed system that allows data to be maintained in local environments, as opposed to using a centralized approach, which would require the consolidation of the data into one physical location. There are at least two key benefits to this approach. First, it supports maintenance of patient privacy by keeping directly identifiable patient information behind local firewalls in its existing protected environment. Next, given that each data system is unique, using a distributed approach means that data owners can be directly involved in running analyses. This involvement will help ensure an informed approach to interpreting results.

With the distributed approach, the signal refinement assessment of a safety signal would be sent to participating data partners, including academic centers, healthcare systems, and medical insurance companies. Participating partners would evaluate the safety signal in their databases and return result summaries. Using active surveillance scientific methodologies, FDA would be able to enhance its understanding of postmarket safety issues to help inform regulatory decisions and, ultimately, healthcare decision-making.

Why is Active Surveillance Needed?

For the past 40 years, *spontaneous reporting* has been the cornerstone of FDA's postmarket medical product safety monitoring effort. The spontaneous reporting system depends on the public — both healthcare professionals and their patients — to *voluntarily report* adverse events,

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[6] U.S. Food and Drug Administration, Guidance for Industry, *Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment*. March 2005. Available at: http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126834.pdf.

errors, and quality problems they may observe during the use of a product to either manufacturers or FDA (manufacturers are required by law to submit to FDA reports they receive of adverse events). Each year, FDA receives over 600,000 adverse event reports on marketed drugs and biological products and approximately 300,000 reports of medical device-related adverse events. Although well-documented observations made at the point-of-care are an invaluable component of FDA's safety surveillance efforts, substantial underreporting of adverse events is widely acknowledged. And of the reports submitted, many are incomplete.

According to the International Conference on Harmonization – guidance for industry, *E2E Pharmacovigilance Planning*, "active surveillance, in contrast to passive surveillance, seeks to ascertain completely the number of adverse events associated via a continuous preorganized process."[7] Active surveillance can be (1) medical product-based, identifying adverse events in patients taking certain products; (2) setting-based, identifying adverse events in certain healthcare settings where patients are likely to come for treatment, e.g., emergency departments; or (3) event-based, identifying adverse events that are likely to be associated with medical products, e.g., acute liver failure.[6] As mandated by Congress in FDAAA, the Sentinel System will focus on medical product-based active surveillance. Frequently, active surveillance methods are conducted in a defined population so that the denominator for the rate of an adverse event can be known.

In the Sentinel System, active surveillance will involve the use of sophisticated statistical and epidemiological methods to actively search for patterns in defined patient populations, such as insurance claims databases or electronic health record systems, which might suggest the occurrence of an adverse event or safety signal related to use of a medical product. The ability to evaluate a defined population in near real-time, as well as compare the medical product of interest to other similar products, rather than depend on an individual's decision to voluntarily report, is what distinguishes this approach from passive reporting.

The active electronic safety surveillance system that will be established through the Sentinel Initiative will seek to complement FDA's current surveillance systems in the following ways:

- Improve capability to identify and evaluate safety issues in near real-time.
- Expand capacity for evaluating safety issues:
  - Improve access to subgroups and special populations, e.g., the elderly;
  - Improve access to longer-term data; and
  - Improve capability to identify increased risks of common adverse events, e.g., myocardial infarction, fracture that healthcare practitioners may not suspect are related to medical products.

[7] International Conference on Harmonization (ICH) – guidance for industry, *E2E Pharmacovigilance Planning. April 2005*. Available at: http://www.fda.gov/RegulatoryInformation/Guidances/ucm129411.htm.

How Have Transparency and Stakeholder Involvement Been Maintained?

With the launch of the Sentinel Initiative in May 2008, FDA expanded existing and established new collaborations with the public and private sectors to evaluate how best to formulate specific short- and long-term plans for establishing the new system to ensure that the process is transparent and that stakeholders remain involved. More than a dozen contracts have been awarded (see Attachment 1); dozens of public meetings and workshops have been held, and key pilot projects have been expanded or initiated (see discussion below and Attachment 2). Key collaborations have been established. Specific details on Sentinel Initiative activities listed can be found in the timeline included as Attachment 2.

From the start, one of our goals has been to learn from and integrate the many relevant activities that already were under way. Among those is SafeRx, a collaboration between FDA and CMS, initiated to leverage the capabilities of these HHS agencies to enhance postmarket safety surveillance and evaluation of FDA regulated medical products. One of the SafeRx projects is helping with near real-time monitoring of seasonal and H1N1 influenza vaccines while providing invaluable lessons that are informing the development of FDA's Sentinel System.

It bears emphasizing that developing and implementing the Sentinel System is a long-term effort that must proceed in stages with very careful planning. It is essential, for example, that the ultimate Sentinel System be implemented in a way that guarantees the integrity of FDA's regulatory and statutory mandates and that the privacy and security of personally identifiable information[8] and other proprietary information remain safeguarded. It is also FDA's goal to ensure that those aspects of the system that should become a shared national resource (e.g., research on methods and underlying data infrastructure) remain accessible. Finally, developing and implementing the Sentinel System will only be possible as the requisite fiscal, human, and technological resources become available.

II. PROGRESS IN MEETING FDAAA GOALS

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 issues, and initiate activities and pilots that would inform such a system. In the attachments to the 2008 *Sentinel Initiative Report*, issued at the launch of the initiative, FDA listed a number of pilots that were in progress in 2008 in the public and private sectors.[9] Many of those collaborations have continued, and new ones have been initiated. As a result, the data access goals set forth in FDAAA are being met. FDA exceeded the congressional goal of being able to access data from 25 million patients by July 2010, and is on target to meet the 2012 congressional goal.

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[8] Defined in an Office of Management and Budget memo dated May 22, 2007, the phrase *personally identifiable information* refers to information that can be used to distinguish or trace an individual's identity, such as their name, Social Security number, biometric records, etc. alone, or when combined with other personal or identifying information that is linked, or linkable, to a specific individual, such as date and place of birth, mother's maiden name, etc. (available at: http://www.whitehouse.gov/omb/memoranda/fy2007/m07-16.pdf).

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

Of special interest in this report are two pilots under way that are directly relevant to development of the Sentinel System and that are already enabling FDA to apply active postmarket risk identification and analysis methodologies to refine specific medical product safety signals and to better understand the outcomes associated with the use of those products.

- The *Mini-Sentinel* pilot, which was launched at the end of 2009, will enable FDA to query privately held automated healthcare data, including administrative and claims data from health plans covering more than 70 million members, with electronic medical records for ~10 million patients, inpatient data from collaborating hospitals, and data from numerous registries.
- The *Federal Partners Collaboration* (FPC) with CMS, the Department of Veterans Affairs (VA), and the Department of Defense (DoD) is enabling FDA to query publicly held automated healthcare data, including administrative and claims data and electronic medical records.

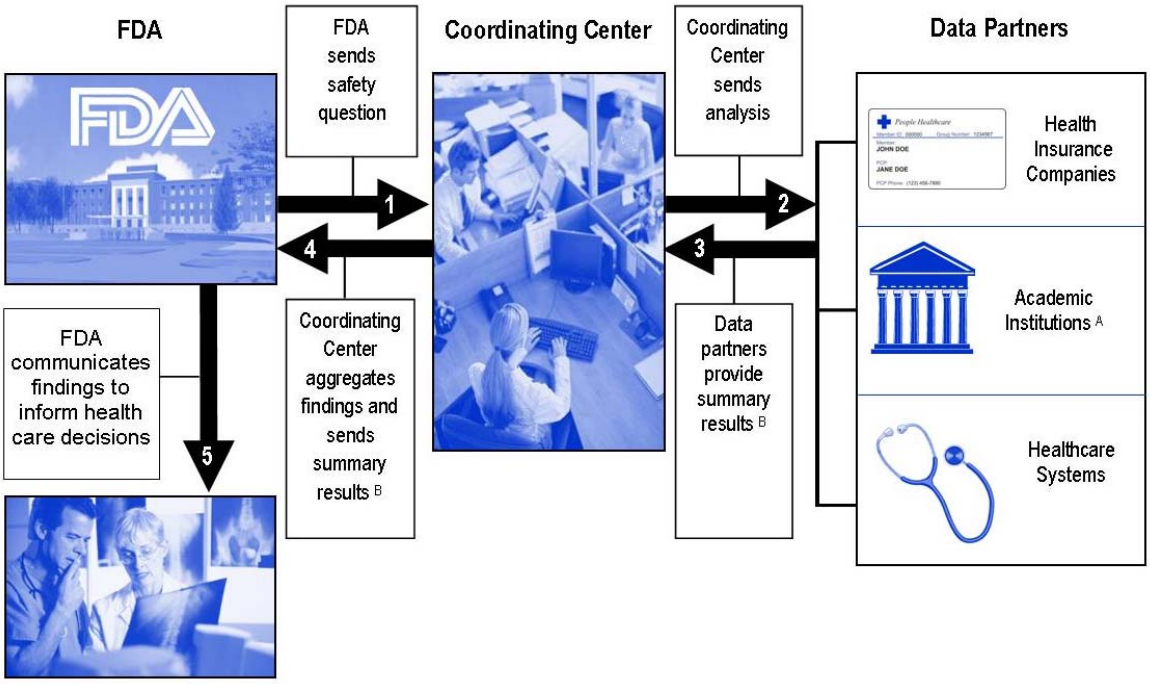
A. A Sentinel System Pilot Program (Mini-Sentinel)

To develop the data infrastructure and scientific operations needed for the eventual Sentinel System, FDA has initiated specific projects that will inform our understanding of the feasibility and utility of methodologies that could be used in an active product surveillance program. In 2009, FDA awarded a contract to the Harvard Pilgrim Health Care Institute (HPHC) to create a coordinating center to lead a consortium of more than 20 collaborators who will help develop a pilot Sentinel System (Mini-Sentinel). Collaborating institutions not only contribute as data partners, but also share expertise in statistical and epidemiological methodologies.[10] HPHC has the necessary expertise and staffing to support FDA in developing the data infrastructure and implementing the specific scientific operations that would be needed for the Sentinel System.

As described in Figure 1, Mini-Sentinel's Coordinating Center has the ability to take FDA-identified questions and submit them to data partners for signal refinement assessments to better understand specific safety signals. Data partners will evaluate the safety signal in their databases, behind established secure firewalls, and return only summaries of results to the Coordinating Center. The *Mini-Sentinel* pilot is creating a kind of laboratory, giving FDA the opportunity to test epidemiological and statistical methodologies in the assessment 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.

[10] The collaborating institutions in the consortium include the following organizations: Aetna; Cincinnati Children's Hospital Medical Center; Brigham and Women's Hospital; Duke University School of Medicine; HMO Research Network (includes Group Health Cooperative, Harvard Pilgrim Health Care Institute, HealthPartners Research Foundation, Henry Ford Health System, Lovelace Clinic Foundation, Marshfield Clinic Research Foundation, Meyers Primary Care Institute); HealthCore Inc; Humana; Kaiser Permanente Center for Effectiveness and Safety Research; 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.

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



A. Only those academic institutions with automated healthcare data will receive safety questions for assessment.

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.

After award of the Mini-Sentinel contract, FDA began working with the contractor to establish the Coordinating Center.[11] This project is in its second year of development. The effort covers all aspects of active medical product surveillance using automated healthcare data, including developing methodologies for identifying signals (signal generation), conducting signal refinement assessments, and performing signal evaluations. Additionally, the challenges of conducting active surveillance in different types of databases are being addressed by developing methods for anonymous linking of databases to improve longitudinal follow-up of patients, as well as accessing information in registries that would enhance surveillance efforts, e.g., cancer registries, device registries, the National Death Index.

In addition, the PRISM program has been incorporated into Mini-Sentinel operations. PRISM was launched by the HHS in collaboration with FDA and CDC for H1N1 vaccine surveillance. Through integration into the Mini-Sentinel pilot, it has been expanded for other vaccine surveillance and to evaluate methodological issues specific to vaccine surveillance.

[11] Available at: https://www.fbo.gov/index?s=opportunity&mode=form&tab=core&id=0caf0580698a82b4a3c87b9564b8965a&_cview=0&cck=1&au=&ck=

The Mini-Sentinel Coordinating Center and participating data partners will use a common data model as the basis for their analytic approach. The approach requires participating data partners to transform their data into a standardized format. This transformed dataset remains with each data partner to form the Mini-Sentinel Distributed Database. With all the data in a common format, the Coordinating Center will write a single program of analytic code for a given safety question, and each participating data partner will run the query in their standardized dataset. Participating organizations will conduct any analyses behind existing secure firewalls and send only summary results to the Coordination Center and FDA for further evaluation.[12] The use of a common analytic program will minimize the potential for differences in results across data holders caused by differences in analytic approach.

As part of its contract, HPHC is assuming responsibility for ensuring that use of data complies with the Health Insurance Portability and Accountability Act (HIPAA). FDA is not requesting specific identifiers for patients, providers, or health plans. Any results sent to FDA will include only summarized or aggregated data in a standard predetermined format. As currently envisioned, all analysis of data will be performed by the data holders in their secure environments without transfer of personally identifiable information.

B. Collaborating with Our Federal Partners

In Section 905 of FDAAA, Congress mandated that FDA, in creating a system for postmarket risk assessment and analysis, work with its Federal partners as well as the private sector to access a variety of electronic health care data. As described below, to meet this requirement, FDA expanded earlier collaborations with CMS to include the VA and DoD.

Since 2002, FDA's Center for Biologics Evaluation and Research (CBER) and CMS have collaborated to evaluate vaccine safety[13] using retrospective (historical) Medicare data for analyses. These efforts expanded in 2006 to include a pilot project with the initial objective of developing a rapid-response system to actively monitor vaccine safety among the elderly using Medicare claims data.[14] The pilot was successful; current efforts focus on developing and evaluating methodological approaches for achieving real-time surveillance. Also in 2006, FDA's Center for Drug Evaluation and Research (CDER) began partnering with the Agency for Healthcare Research and Quality to develop data structures and methodologies for identifying and analyzing adverse drug events using Medicare Part B data.

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[12] Although data holders will do their own analyses and provide only summary results to the coordinating center, there may be circumstances in which there will be a need for transmission from current data holders to the Coordinating Center of information that could be characterized as protected health information (e.g., responses from data holders that would be considered *small cells*). FDA is considering options to ensure HIPAA compliance in those situations.

[13] Initial funding was provided by the HHS National Vaccine Program Office for a joint FDA-CMS project (*Use of Medicare Data to Evaluate Adverse Events after Influenza or Pneumococcal Vaccine*). For additional information about this project, see Burwen DR, La Voie L, Braun MM, et al. "Evaluating adverse events after vaccination in the Medicare population," *Pharmacoepidemiology and Drug Safety*, 2007; (16): 753-61.

[14] Funding for this work was provided by HHS's National Vaccine Program Office (*Rapid Assessment of Vaccine Safety Using Medicare Data*) and by CMS through a contract supporting construction of research files (performed by the firm Acumen LLC).

These initial activities formed the foundation for the SafeRx Project, which was officially launched in 2008 when the Medicare Part D (prescription drug benefit) data became available for research purposes. With initial financial support from the Assistant Secretary for Planning and Evaluation for HHS, SafeRx established collaborations between CMS and multiple FDA centers, including CBER, CDER and the Center for Devices and Radiological Health. FDA's participation in the SafeRx project was initially planned by the Sentinel Team.

These collaborations have included exploratory analyses, full epidemiological studies, and active surveillance assessments. The projects that have the most relevance for the development of the eventual Sentinel System include the following:

- *Real-time surveillance of vaccines*: SafeRx has developed, and is currently operating, a real-time surveillance system monitoring the recent flu pandemic and seasonal influenza vaccine.
- *Postmarket surveillance of medical products*: SafeRx has undertaken assessments monitoring the use of drug, biologic, and device products and evaluating some specific safety concerns. Access to real-time data has also enabled SafeRx to evaluate the use of newly marketed drugs.

These types of projects illustrate the existing capacity of SafeRx to conduct safety assessments for a wide range of medical products. Medicare and Medicaid claims provide rich data sources for meeting FDA's goals of monitoring medical product use and safety considerations in important patient populations. However, it is clear that only by expanding the populations in which medical product safety is monitored will the safety profiles of those products be thoroughly understood.

The FPC, launched in 2009, involves creating a distributed system that leverages the work already being undertaken with CMS in the SafeRx project. The FPC is similar to the Mini-Sentinel pilot in that it uses an active surveillance approach and involves a distributed system. However, unlike Mini-Sentinel, which is using a common data model, the FPC is using a common active surveillance protocol, and then each Federal partner writes analytic code to run the protocol in its own database. Lessons learned from this pilot will be compared to lessons learned by the Mini-Sentinel model. Such a comparison will enable FDA to identify the potential benefits and drawbacks of both approaches. Additionally, FDA can learn more about how to interpret active surveillance findings within systems with differing practice patterns and among populations with differing demographic characteristics and health conditions.

C. Sentinel System — Security and Privacy

Safeguarding the privacy and security of all information FDA receives is of paramount concern to the Agency — and a fundamental aspect 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 initiative involved identifying and analyzing potential privacy issues.

As already explained, FDA is working towards establishing a *distributed system*. As currently planned, no personally identifiable information will be transferred to FDA. Personally identifiable information will, with rare exceptions, remain under the local control of participating data partners, behind existing firewalls, protected by established privacy and security safeguards. Because of the unique characteristics of each data owner's database and system and because of changes that may occur in a specific healthcare system that can affect how data is captured, FDA believes that the data partner is best situated to run analyses and understand and interpret resulting findings. Those data partners who wish to participate in the Sentinel System will perform analyses of their own data upon request and provide only summary results to the Coordinating Center and FDA.

As we have begun to grapple with the realities of conducting active medical product surveillance, however, we have come to understand that there may be infrequent occurrences when de-identified datasets[15] may be insufficient to meet the needs of medical product surveillance. Some circumstances may require the sharing of information between or among data partners and/or with the Coordinating Center. Therefore, FDA is actively exploring methods and techniques that will meet the needs of these specific types of active surveillance assessments while ensuring full compliance with HIPAA protections. FDA is actively engaged with privacy experts to explore what other approaches for consumer protection should be developed or expanded.

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). Because the Sentinel System is being sponsored by FDA and is being established in response to FDAAA, the System must be assessed as part of the FDA Certification and Accreditation (C&A) process as required by FISMA. The C&A process, milestones, and project plan will be provided by the FDA Security Office and executed by FDA Security Office contractors once the environment is ready.

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[15] The following identifiers of the individual or of relatives, employers, or household members of the individual must be removed to achieve the *safe harbor* method of de-identification as described in applicable HIPAA regulations: (A) Names; (B) All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of Census (1) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (2) the initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000; (C) All elements of dates (except year) for dates directly related to the individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older; (D) Telephone numbers; (E) Fax numbers; (F) Electronic mail addresses: (G) Social security numbers; (H) Medical record numbers; (I) Health plan beneficiary numbers; (J) Account numbers; (K) Certificate/license numbers; (L) Vehicle identifiers and serial numbers, including license plate numbers; (M) Device identifiers and serial numbers; (N) Web Universal Resource Locators (URLs); (O) Internet Protocol (IP) address numbers; (P) Biometric identifiers, including finger and voice prints; (Q) Full face photographic images and any comparable images; and/or any other unique identifying number, characteristic, or code, except as permitted for re-identification purposes provided certain conditions are met. In addition to the removal of the above-stated identifiers, the covered entity may not have actual knowledge that the remaining information could be used alone or in combination with any other information to identify an individual who is subject of the information. 45 CFR 164.514(b).

Because the System will use a distributed data model, this provides additional protections to ensure that there are no security breaches resulting in disclosure of personally identifiable information. FDA recognizes, however, that attention will need to be paid to computer security with respect to the transmission of queries and results summaries, and policies and procedures will need to be developed and implemented to ensure computer security at each stage of the process.

One of the initial tasks of the Mini-Sentinel pilot was to consider approaches to ensure compliance with laws and regulations related to privacy and protection of electronic healthcare data being used for medical product surveillance. To accomplish this, Mini-Sentinel formed a Privacy Panel, consisting of experts in the field. A report was issued by this group that addresses compliance under the Common Rule[16] and HIPAA[17] for data partners participating in Mini-Sentinel.[18]

III. CONCLUSION

FDA has welcomed this opportunity to report to Congress on the Sentinel Initiative, its rapid progress, and its accomplishments. Although developing and implementing the Sentinel System is a long-term, scientifically and technologically very challenging undertaking, we can report significant progress under the Initiative, and we are committed to continuing this ambitious pace during the coming years.

With the Initiative's launch, FDA created a broad public forum — essential to the success of a program of this size and complexity. Many contracts have been bid and awarded to inform the development of the Sentinel System, especially in the areas of scientific operations, data infrastructure, governance, and privacy. Two important pilots were launched in the Fall of 2009: *Mini-Sentinel* with participants from the private sector; and the FPC with FDA, CMS, VA, and the DoD. Both pilots will directly inform the Agency on the best approaches for designing and developing the Sentinel System. The 2010 goal set by Congress in section 905 of FDAAA to achieve access to data from 25 million patients was met and exceeded, and FDA is on target to meet Congress's 2012 goal. Building on experience gathered through SafeRx and other collaborative efforts, the Mini-Sentinel pilot and the FPC pilot are enabling FDA to leverage the power of large amounts of private and public health care data, respectively, and to work with voluntary participants to test, in near real-time, the analytical tools and methodologies that are being developed for use in active surveillance and will be used once the Sentinel System is in place. Last but not least, concerns raised by numerous stakeholders — including how to guarantee the privacy and security of personally identifiable information — are being addressed to ensure that all relevant protections are maintained.

As FDA continues its efforts to develop a Sentinel System as a tool to conduct active

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[16] 45 CFR part 46

[17] Pub. L. No. 104-191, 110 Stat. 1936 (codified as amended at scattered sections of 18, 26, 29, 42 U.S.C.).

[18] The report *HIPAA and Common Rule Compliance in the Mini-Sentinel Pilot* is available at: http://mini-sentinel.org/work_products/About_Us/HIPAA_and_CommonRuleCompliance_in_the_Mini-SentinelPilot.pdf.

surveillance on the medical products that the Agency regulates, we are aware of the system's potential value to other public and private entities. A system such as Sentinel should not be created for the exclusive use of just one agency; rather, it should be developed in such a way as to make it a national resource for all stakeholders in the healthcare system, providing maximal value to public health in the broadest sense of the term. FDA envisions that one day the Sentinel System will be part of a larger national infrastructure that will help meet the needs not only of regulators, but also of academicians and the regulated industry — available for use by those interested in the safety of medical products and those interested in healthcare quality.

The Sentinel Initiative is providing an opportunity for the broad medical and scientific communities to partner in the establishment of a significant foundation for future research. FDA is enabling the collaboration needed to make this vision a reality through its outreach to other government agencies and the private sector, with the goal of achieving economies of scale, reducing duplication of efforts, and leveraging available human and financial resources. This type of collaboration is critical to Sentinel's success.

Throughout this effort, FDA has been extremely vigilant to ensure that the Sentinel Initiative and related efforts are progressing in the most transparent way possible with extensive public and private participation. Because of the many technical, scientific, and policy challenges involved, the Initiative cannot succeed without the full participation of stakeholders in the healthcare community.

ATTACHMENT 1. PRODUCTS FROM CONTRACTS AND COOPERATIVE AGREEMENTS TO INFORM THE DEVELOPMENT OF THE FDA SENTINEL SYSTEM

The following documents have resulted from contracts awarded to inform the development of the FDA Sentinel System and are now available in the FDA Docket (Docket ID: FDA-2009-N-0192)[19] and on the Sentinel Initiative Website.

- *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 Institute report.
- *Evaluation of Existing Methods for Safety Signal Identification*, a Group Health Cooperative Center for Health Care 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*, an 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.
- *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.

Work on the following projects is still ongoing under existing contracts or cooperative agreements.

- *Detection and Analysis of Adverse Events to Regulated Products in Automated Healthcare Data: Efforts to Develop the Sentinel Initiative*, a collaboration led by the Harvard Pilgrim Health Care Institute.
- *Convener of Active Medical Product Surveillance Discussions*, a series of public and expert panel meetings convened by The Brookings Institution.

[19] Available at Regulations.gov at: http://www.regulations.gov/#!docketDetail;D=FDA-2009-N-0192

ATTACHMENT 2. SENTINEL INITIATIVE MILESTONES

March 2007	FDA holds two-day public meeting on concept of creating a nationwide system for monitoring medical product safety that garners overwhelming support.
Sept. 2007	Congress passes FDA Amendments Act of 2007 (FDAAA) requiring FDA to collaborate with public, academic and private entities to develop methods to obtain access to disparate data sources and validated means to link and analyze safety data. FDAAA mandates active postmarket risk identification "with respect to a drug approved under this section [section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C 355)] or under section 351 of the Public Health Service Act" and also sets "goals of including, in aggregate at least 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, data holders, vendors, regulated industry).
May 2008	FDA launches Sentinel Initiative and issues a report outlining the program and its goals.
May 2008	FDA-CMS-ASPE launch SafeRx, building on existing collaborations with CMS and AHRQ, enabling among other projects, near real-time safety monitoring of seasonal and H1N1 influenza vaccines.
June 2008	Sentinel Team establishes Federal Partners Working Group, which meets quarterly to explore issues related to the Sentinel Initiative and other complimentary initiatives within HHS.
Aug-Sept. 2008	Sentinel Team awards 8 contracts to inform the development of the Sentinel System by addressing issues related to governance, privacy, data and infrastructure, scientific operations, and outreach (see Attachment 1).
December 2008	Sentinel Team and eHealth Initiative Foundation cosponsor the public workshop *Sentinel Initiative: Structure, Function and Scope*, in cooperation with Brookings Institution. Stakeholders participating include academia, data holders, vendors, consumers, patient representatives, Federal partners and industry.
Sept. 2009	Sentinel Team awards a cooperative agreement to Brookings Institution to convene multiple discussions on topics related to active medical product surveillance.
Sept. 2009	Sentinel Team awards 3 contracts to inform the development of the Sentinel System by addressing issues related to privacy, operations, and data for veterinary medicine safety surveillance (see Attachment 1).
Sept. 2009	Sentinel Team awards a contract to Harvard Pilgrim Health Care Institute to create Mini-Sentinel with a Coordinating Center to support the development of the scientific operations needed for the Sentinel Initiative.
Sept. 2009	Federal Partners Collaboration is launched to create a pilot that includes FDA, CMS, DoD, and the VA to develop a distributed system that can mirror what FDA envisions doing on a larger scale with the Sentinel System.
Jan. 2010	2nd 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.

July 2010	FDA access to data representing 25 million patients meets 2010 congressional goal.
Sept. 2010	Post-Licensure Rapid Immunization Safety Monitoring (PRISM) program is incorporated into Mini-Sentinel operations to support vaccine surveillance.
Jan. 2011	3rd Annual Sentinel Initiative Public Workshop is convened by the Brookings Institution's Engelberg Center for Health Care Reform and supported by a grant from FDA.
Feb. 2011	Under Mini-Sentinel, implemented capability to conduct rapid response safety queries in the Mini-Sentinel Distributed Database.