MINI-SENTINEL SYSTEMATIC VALIDATION OF HEALTH OUTCOME OF INTEREST

ACUTE MYOCARDIAL INFARCTION CASES REPORT

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I. EXECUTIVE SUMMARY

A. OVERVIEW OF PROJECT

The U.S. Food and Drug Administration's (FDA) Mini-Sentinel is a pilot program that aims to conduct active surveillance to refine potential safety signals of marketed medical products. The purpose of this Mini-Sentinel task order activity was to develop and design an abstraction and adjudication process that can be used when full text medical record review is required to confirm a coded diagnosis and to test this approach by validating a code algorithm for acute myocardial infarction (AMI). This workgroup aligned closely with efforts being pursued by the AMI Active Surveillance Workgroup.

The AMI validation project consisted of four parts: (1) **case identification**, in which an ICD-9-CM-based algorithm was developed to identify hospitalized AMI patients within the Mini-Sentinel Distributed Database; (2) **chart retrieval and extraction**, in which a procedure was established to ensure patient privacy, collecting and transferring the minimal amount of de-identified information needed to validate potential cases of AMI; (3) **abstraction and adjudication**, in which trained abstractors gathered key data using a standardized form and cardiologists carried out protocol-driven adjudication; and (4) **calculation of the positive predictive value (PPV)** of the constructed algorithm.

B. SUMMARY OF FINDINGS

Key decision points focused on: (1) the breadth of the AMI algorithm; (2) centralized vs distributed abstraction; and (3) approaches to maintaining patient privacy and to addressing the project's status as a public health activity that does not come under the purview of Institutional Review Boards (IRBs). An algorithm limited to ICD-9-CM codes 410.x0-410.x1 was used. Centralized data abstraction was performed for efficiency due to the modest number of medical chart abstractions (maximum of 153 charts distributed across Data Partners). The project's public health surveillance status facilitated chart retrieval in most instances. A high percentage of charts (143 out of 153, or 93%) were obtained, with greater than 85% of charts from participating Data Partners providing all critical components for AMI validation. There was great variability by Data Partner in the size of the chart extract obtained. Data Partners provided chart extracts with on average as few as 45 pages and on average as many as 344 pages per chart. Overall the PPV was 86.0% (95% confidence interval, 79.4% to 90.8%).

C. RECOMMENDATION FOR VALIDATION APPROACH AND SUGGESTION FOR FUTURE INVESTIGATIVE EFFORTS

The algorithm developed by the workgroup for identifying cases of AMI (ICD9-CM code 410.x1 or 410.x0 in the principal or primary position) has an overall PPV of 86%. This overall PPV is somewhat lower than the experience reported in prior studies. Many of these older studies did not employ the universal definition of myocardial infarction, and did not consider the evolving consensus regarding troponin levels, as they relate to this definition. A PPV of 86% may be considered adequate for some surveillance activities relevant to medical product safety, but not for others. Future validation studies of AMI should consider assessing the impact on the PPV of incorporating additional criteria into the algorithm (e.g., length of stay and hospital transfer criteria).

Based on the findings of the AMI validation project, we recommend a centralized approach for the abstraction and adjudication of health outcomes of interest when only a modest number of cases are

being validated across multiple Data Partners. A centralized approach to these activities lends efficiency in the training of abstractors and enhances quality control.

II. BACKGROUND

In 2007, the U.S. Congress passed the FDA Amendments Act (FDAAA) mandating the FDA to establish a postmarket surveillance system using electronic health data from multiple sources.[1] In May 2008, in response to the Congressional mandate, the FDA launched the Sentinel Initiative, a long-term program designed to create a national electronic monitoring system for medical product safety (the Sentinel System). The Sentinel System is being developed and implemented in stages and, when fully functional, will complement FDA's existing postmarket safety surveillance systems.

The Mini-Sentinel pilot, a contract awarded by FDA to Harvard Pilgrim Health Care Institute (HPHCI) to develop the scientific operations needed for the eventual Sentinel System, is being conducted as a collaborative effort between FDA and a consortium of institutions led by HPHCI.[2-3] Since accurate and timely identification of health outcomes of interest (HOIs) is an essential component of active safety surveillance, Mini-Sentinel convened a workgroup to establish a process for identification and validation of a selected HOI: AMI. This is the first HOI to be validated under Mini-Sentinel. In addition to developing and validating an algorithm to identify hospitalized AMI cases within the Mini-Sentinel Distributed Database,[4] another goal of the workgroup was to design an efficient validation process that could be used as a model for future validation efforts of other HOIs.

The remainder of this report is structured as follows. In the Methods section below, the AMI Validation Workgroup's development of the Mini-Sentinel validation process for AMI will be reviewed and the challenges encountered will be discussed. In the Results section, the findings from abstraction and adjudication activities relevant to this project will be presented.

III. METHODS

A. OVERVIEW OF DESIGN FOR THE AMI VALIDATION PROCESS

The Mini-Sentinel AMI Validation project was a collaboration between the FDA, the Mini-Sentinel Operations Center (MSOC), and selected Academic and Data Partners. The role of each collaborator is outlined in Appendix A. Four Mini-Sentinel Data Partners participated in this project: (1) HealthCore, Inc.; (2) Humana; (3) three member health plans within the Kaiser Permanente Center for Effectiveness and Safety Research; and (4) two member health plans within the HMO Research Network.

The AMI validation process consisted of four components: (1) an approach to **case identification** with the goal of producing an ICD-9-CM-based algorithm that would reliably identify patients hospitalized for AMI within the Mini-Sentinel Distributed Database; (2) a protocol for **case retrieval** from the Data Partners, which outlined the minimum necessary chart components to confirm the AMI diagnosis and systematized approaches to obtaining and de-identifying chart information; (3) a parsimonious data **abstraction** instrument including relevant elements derived from the medical chart components and completed by trained nurse abstractors; and (4) an **adjudication** protocol for confirmation of the AMI diagnosis by cardiologist adjudicators. The culmination of this effort is a determination of the **PPV of the algorithm**.

B. CASE IDENTIFICATION

The goal of this Mini-Sentinel activity was to validate the diagnostic codes used to identify likely AMI cases across all Data Partners. It was determined that approximately 100 charts would be sufficient to obtain an overall assessment of the PPV, although it was understood that this limited sample would be insufficient to evaluate the sensitivity of the PPV across a full range of scenarios relating to Data Partners and patient characteristics. To have the findings of this effort be as contemporary as possible, this activity included only patients who were hospitalized for AMI between January 1, 2009 and December 31, 2009 within the Mini-Sentinel Distributed Database, which currently comprises administrative and claims data formatted into a common data model.[4] There were no restrictions on age, sex, other diagnoses, or other patient characteristics, but patients were required to be enrollees of the health plan for the entire duration of hospitalization.

The AMI Validation Workgroup had the opportunity to consult with a concurrent Mini-Sentinel workgroup that was charged with developing an active surveillance protocol for AMI.[5] The two workgroups began by reviewing the literature and examining prior completed reviews to identify previously used algorithm components, with a focus on those yielding the highest PPVs (Appendix B).[6-7] Clinicians, including cardiologists, cardiovascular researchers, and FDA staff with expertise in cardiovascular disease were also consulted. The team considered the types of clinical information that would likely be available from medical records relating to a hospitalization for AMI, as well as the likelihood of access to information both prior to the hospitalization and following hospital discharge for AMI survivors. The group reviewed the pathophysiology of AMI and acute coronary syndrome (ACS), and considered whether to create a narrow definition of AMI or a definition that would more broadly capture a spectrum of clinical conditions reflecting acute myocardial ischemia (ACS).

In reviewing the literature, a wide range of ICD-9-CM codes were found to be in use, with a limited number of studies assessing ICD-8 or ICD-10 codes and several studies combining ICD codes with other criteria.[6-19] The ICD-9-CM code 410 (AMI) was identified as the code most frequently employed, yielding PPVs in the mid to high 90% range, and the need to specify the ICD-9-CM code using two decimal places was considered. Since the number 2 in the second place after the decimal (i.e. 410.x2) indicates a past MI, the sample was limited to 410.x0 or 410.x1 (Appendix C). Although previously studied algorithms that incorporated hospital length-of-stay were assessed, the team did not find that this reliably increased the PPV and, therefore, did not include a length-of-stay criterion in the final algorithm.[9, 11, 15-16]

The workgroup also considered including deaths occurring within one day of an emergency department visit for acute ischemic heart disease (ICD-9-CM code: 411.1, 411.8, 413.x) in the definition, but decided against including these additional ICD rubrics due to concerns regarding the adequacy of information that would be available to adjudicate these cases. The final algorithm to identify AMI patients identified patients with ICD-9-CM principal (or first-listed) discharge codes 410.x0 and 410.x1 (Appendix D).

Based on this algorithm, the Operations Center developed a SAS program, tested it with two Data Partners for accuracy, and then distributed it to all Data Partners participating in the project. In order to identify a random sample of AMI cases and the hospitals in which they received care, participating Data Partners executed the SAS program to query their own locally maintained administrative and claims data (see following section of this report). Mini-Sentinel uses a distributed data approach in which Data Partners maintain physical and operational control over electronic data in their existing environments. Data Partners execute standardized programs provided by the Operations Center and then share the

output of these programs, typically in summary form, with the Operations Center. Data Partners transform their data into the Mini-Sentinel Common Data Model (MSCDM) format in order to standardize administrative and clinical information across Data Partners prior to running the SAS programs. To obtain approximately 100 cases for eventual adjudication, efforts were made to identify 153 cases distributed across all participating Data Partners, with each participating Data Partner pursuing an equal number of cases.

C. CASE RETRIEVAL

The workgroup developed a protocol for retrieving medical chart information. In order to proceed with chart retrieval, the group needed to: (1) determine whether chart abstraction would take place centrally or in a locally distributed fashion (i.e., having each Data Partner abstract its own charts); and (2) establish protocols for ensuring the privacy and security of data and for explaining the status of this effort as a public health surveillance activity not under the oversight of IRBs.

Because the abstraction process chosen would have major implications in terms of the amount of information to be transferred for centralized abstraction, the workgroup held multiple meetings to address the question of centralized vs distributed data abstraction. Before selecting an approach to pursue, the group discussed why a centralized versus distributed approach might be preferred for the purpose of this validation activity and as a model for future Mini-Sentinel validation efforts.

1. Centralized vs distributed chart abstraction

In considering which approach to pursue, the workgroup discussed a number of issues. These included: (i) **the ability to maintain patient privacy**; (ii) **the existing infrastructure within the Data Partners to perform medical chart abstractions by trained abstractors**; (iii) **the quality of data abstraction**; (iv) **short-term efficiency**; and (v) **long-term efficiency**.

- **Capacity to maintain patient privacy**: Although all information would be de-identified prior to transmission to a centralized Operations Center, Data Partners noted that with a centralized approach, the amount of chart information transferred could challenge the ability to maintain de-identification. There were also concerns that the greater the amount of medical record materials to be redacted, the greater the chance that some individually identifiable health information might fail to be redacted.

- **Existing infrastructure within the Data Partners to perform medical chart abstraction by trained abstractors:** Some Data Partners advocated for a distributed approach since they already had available experienced abstractors who could be trained to perform the required abstraction tasks.

- **Quality of data abstraction:** Given the modest number of medical records to be located and abstracted per site and the relatively high number of sites, it would be challenging to train abstractors to perform only a handful of abstractions and still maintain adequate quality and reliability of these abstraction efforts in an ongoing manner. In addition, some Data Partners would not be using nurses and/or other individuals with relevant healthcare experience as abstractors, leading to increased risk of variation in abstraction quality.

- **Short-term efficiency:** A distributed approach would require abstractor training and evaluation at multiple sites, potentially impacting the timeline for the overall abstraction effort.

- **Long-term efficiency**: Efficiency of future Mini-Sentinel validation projects was also a consideration. In the future, when a new HOI needs to be validated, a centralized approach would require training of a limited number of abstractors, instead of periodically retraining multiple abstractors distributed across the multiple Data Partners. A centralized approach could maximize resources and minimize the amount of time required to abstract necessary information.

After careful consideration, a centralized approach was ultimately pursued; selected components of medical records were extracted and redacted of individually identifiable information locally, before they were securely transferred via the Mini-Sentinel Secure Portal to the lead team, at Meyers Primary Care Institute, for centralized abstraction.

2. Determination of chart components

Once a centralized abstraction approach was chosen, the lead team proposed a list of the critical chart components and other information they considered important for the AMI validation. This initial list was developed broadly and then narrowed down based on input from: Data Partners, the Operations Center, the FDA, and individuals with clinical and epidemiologic expertise relevant to cardiovascular disease.

Abstraction tools from various cardiovascular surveillance studies were reviewed to inform decisions on the list of critical chart components and other information to be extracted.[20] In response to Data Partners' concerns over the amount of information to be extracted and transferred, the lead team narrowed the list of requested items to the following: admission history and physical; discharge summary; transfer records; cardiology consult notes; autopsy reports/death notes; EMT/ambulance notes; emergency department notes; all 12 lead electrocardiograms; laboratory reports; cardiac catheterization reports; percutaneous coronary intervention reports; cardiac bypass surgery reports; cardiac stress test/nuclear stress test reports; and echocardiogram reports (See Appendices E and F for extraction form and manual).

The Operations Center reviewed the revised list in relation to the HIPAA Privacy Rule's minimum necessary standard, and confirmed that the critical chart components and other information requested constituted the minimum necessary amount of information for the activity.

Certain items requested remained broad in scope. For example, copies of all laboratory results were requested. This was done in order to obtain cardiac biomarker information. Cardiac biomarkers are one of the critical items of interest for AMI validation, but only represent a subset of all laboratory results. This decision was made in order to avoid the need for a highly trained individual at each site capable of determining which specific pages of the laboratory report section of the medical record were required.

3. Obtaining chart information

After the list of chart components to be requested was finalized, Data Partners proceeded to execute the SAS program, identifying a random sample of likely AMI cases, whose medical records were to be located. Data Partners then asked source data holders (e.g., individual hospital medical records

departments) for access to the records for these patients. Source data holders either sent the medical records to vendors commissioned to extract, copy, and redact the requested information, or allowed Data Partners direct access to records for extraction, copying, and redaction. Redacted chart data were sent to the Operations Center via the Mini-Sentinel Secure Portal.

The Operations Center provided each Data Partner with a privacy packet prepared by the Mini-Sentinel Privacy Panel (Appendix G). This packet included: (1) the Mini-Sentinel Privacy Panel White Paper describing data privacy issues in Mini-Sentinel; (2) a letter from the Department of Health and Human Services' Office for Human Research Protections (OHRP) to the FDA stating that the regulations OHRP administers do not apply to the Sentinel Initiative (OHRP oversees all IRBs); and (3) a letter from the FDA to the Mini-Sentinel Principal Investigator stating that Mini-Sentinel is a Sentinel Initiative activity. The privacy packet described the legal basis for determining that the work of the Mini-Sentinel pilot constituted a public health activity not under the purview of the IRB. Data Partners were asked to disseminate this information to their IRBs and Privacy Boards as well as any other relevant entities. The Operations Center also provided an instructional flowchart and customizable letter template to provider sites in the activity protocol. The letter (addressed to each provider site from specific Data Partners) explained the purpose of the project and explained what was being requested. Letters also explained that the request was being carried out on behalf of Mini-Sentinel and the FDA (Appendix H). The flowchart outlined the array of possible scenarios for chart retrieval and detailed the steps for chart redaction and data transmission (Appendix I).

Redaction of individually identifiable information was performed in accordance with HIPAA's provisions for a 'limited dataset,' which is an alternative to using fully de-identified information. Under HIPAA, creation of a limited dataset requires removal of 16 direct identifiers, but allows for the inclusion of dates, geographic location (not as specific as street address), and any other code or characteristic not explicitly excluded.[21] Redaction was completed before the chart components were transferred to the Operations Center. Each Data Partner assigned a new, de-identified ID unique to each redacted chart prior to transferring extracted data, and maintained a crosswalk between the newly assigned IDs and the original IDs. Admission and discharge dates as well as dates corresponding to EKGs, laboratory results, procedures and tests were not redacted. This information was considered crucial for determining whether available EKGs and test results corresponded to the hospital stay of interest and therefore whether an AMI occurred during the identified hospital stay. In addition, for certain tests (EKGs, cardiac biomarkers), the results needed to be assessed by cardiologist adjudicators in chronological order. We considered assigning reference values for every date. Ultimately we opted not to pursue this approach since we felt that this would substantially increase workload and introduce multiple opportunities for error.

Data Partners were provided with credentials to login to the Mini-Sentinel Secure Portal for transferring, managing, or retrieving chart components. Security was managed within the folder structure of the site; the Secure Portal contains private folders accessible only to specified members within each Data Partner site and authorized Operations Center staff, as well as common folders defined for all users. Data Partners electronically uploaded redacted charts to their site-specific private folders. The Operations Center verified that all charts were redacted thoroughly and then moved all files to a separate private folder, allowing the lead team access to the data. While the Operations Center is allowed to receive un-redacted medical chart data based on Mini-Sentinel's status as a public health surveillance activity,[22] every effort was made to de-identify the data prior to its transmission to the Operations Center. Redaction was incomplete, however, in two cases. In these instances, the Operations

Center immediately deleted all copies of the data from the Secure Portal, including backup files, and notified the appropriate Data Partner to correct the redaction and resend the data (Appendix J). This ensured that the privacy of patient data was maintained.

4. Challenges encountered during the chart retrieval process

Regarding level of burden, Data Partners were initially concerned that they would be required to obtain information from multiple sources, including outpatient medical records. However, clinical information relevant to the present validation study was to be extracted from medical records relating to only a single hospitalization.

Regarding privacy issues and IRB concerns, Data Partners described several challenges encountered during the chart retrieval process. Though sometimes causing delays, most source data holder IRBs allowed charts to be located and retrieved after being provided with the privacy packet containing letters and documents that clarified the status of this validation project as a public health surveillance activity undertaken under the auspices of the FDA. However, despite the privacy packet, seven charts requested were not obtained due to IRB concerns, and insistence on patient consent before releasing medical records.

Several other issues were brought to the workgroup's attention by the Data Partners. The timing of requests (during December and January) impacted to some extent on overall project efficiency due to holiday-related personnel issues at the facilities holding the medical charts. Some redacted chart extractions were sent by mail as opposed to electronic transmission, which led to delays in transferring data. One Data Partner found that including a list of frequently asked questions and answers (Appendix K) along with each chart request led to improved turnaround times. Frequent inquiries concerning the disposition of charts and relationship building with the hospital staff processing the request were also helpful in obtaining charts more quickly.

In an effort to gather more information about the extraction process, a survey was circulated to each participating Data Partner (Appendix L). This survey was used to capture varying approaches to requesting and retrieving data. Data Partners were also asked about the methods used during the redaction process as well as the approach to overall management.

According to survey responses, Data Partners retrieved charts both electronically and physically, depending on individual circumstances. Most Data Partners instructed their extractors to retrieve only the chart components listed on the extraction form; however, some requested full charts from data holders to ensure that all relevant chart information was received. One site that requested full charts filtered through each chart and sent only the requested components to the Operations Center, while another sent entire charts to the MSOC to ensure completeness and stay within the project timeline. Sending the entire record did not comply with Mini-Sentinel policies. The organization was notified not to send the complete record in the future. These larger charts became a challenge in the abstraction process due to the increased time required to complete abstractions.

Designated staff at each Data Partner completed chart redactions internally. Redactors were initially instructed to remove all patient and provider identifiers in accordance with the HIPAA Privacy Rule.[21] However, as the abstraction form was finalized, the workgroup requested that dates in the chart (i.e. lab dates, procedure dates, admission and discharge dates) not be redacted. Those sites that still had

outstanding chart requests were able to implement this change and send charts redacted according to the revised criteria. Each site performed quality checks on the redacted charts prior to uploading them to the Mini-Sentinel portal.

D. ABSTRACTION

Redacted components of the medical record were sent to the Operations Center via the Mini-Sentinel Secure Portal and then were made available through this website to the lead team for data abstraction by trained nurse abstractors.

The lead team identified and reviewed a number of AMI abstraction forms and manuals used in past surveillance research activities relevant to AMI. The team also consulted with individuals with clinical and epidemiologic expertise relevant to cardiovascular disease, reviewed the American Heart Association (AHA)'s Universal Definition of Myocardial Infarction,[23-24] reviewed the literature on troponin standardization,[25] and communicated with directors of laboratories on percentile cutoffs for what were considered to be "positive" troponin values. Based on clinical consultation and literature review, the lead team created a 36-item **abstraction form** (Appendix M) that included: (a) general demographic information; (b) brief medical history; (c) cardiac biomarker information; (d) copies of electrocardiograms; (e) cardiac testing, procedure, and intervention information; and (f) information on disposition at the time of hospital discharge. The lead team trained two nurse abstractors to enter abstracted information into a Microsoft Access database and provided an accompanying instruction manual (Appendix N). Both abstractors gathered data from the first ten cases. These abstractions were reviewed together with both nurse abstractors to ensure high inter-rater reliability on items critical for the adjudications.

One of the more challenging issues that emerged in the design of the abstraction and adjudication forms related to differences in cardiac biomarker reference standards among different hospitals. It was essential to design abstraction materials that could adequately capture both biomarker results and reference standards, even when presented in a variety of ways from different sources.

The workgroup was also challenged with reconciling the biomarker standards described in the published AHA definition of AMI with laboratory values likely to be available in hospital records.[23] While the AHA definition defined abnormal biomarker values as falling "above the 99th percentile of the upper reference limit," preliminary reviews of several charts showed that hospital laboratories did not routinely report percentile cut-offs. Through communication with the director of one hospital laboratory, the lead team also found that the reported reference values did not always correspond to this 99th percentile cut-off. While the team did capture any and all available information on reference standards from charts (i.e., from printed laboratory reports), laboratories were not contacted for any further clarifying information.

E. ADJUDICATION

In consultation with FDA staff and individuals with clinical and epidemiologic expertise relevant to cardiovascular disease, the lead team created an adjudication protocol based on the AHA Universal Definition of Myocardial Infarction (Appendix O). In addition to abstracted data described above, adjudicating cardiologists were provided with copies of electrocardiograms and copies of all cardiac tests and procedure reports.

Two cardiologists independently reviewed each abstracted case. Cases were classified as (1) definite myocardial infarction (MI); (2) probable MI; (3) no MI; or (4) unable to determine. When the adjudicators disagreed on the classification of a case, they met and reached consensus. Categories (1) and (2), and categories (3) and (4) were combined into single categories in relation to the consensus process. Consensus was reached in all cases. The initial assessment of the adjudicators was compared and inter-rater reliability was calculated using the kappa statistic. This kappa score was found to be 0.60 (95% confidence interval, 0.42 to 0.78).[26] A kappa score of 0.2-0.4 reflects "fair agreement," 0.4-0.6 "moderate agreement," 0.6-0.8 "substantial agreement," and above 0.8 is "almost perfect".[27]

IV. RESULTS

A. CASE RETRIEVAL RESULTS

1. Percent of charts obtained

The total number of charts requested was 153 and we were able to retrieve 93.5% (143 charts). Seven charts were not obtained due to IRB issues (IRBs required patient signature to release charts) and three charts were not obtained because the charts could not be located. Retrieval rates were fairly consistent across the Data Partners, as depicted in Figure 1. See also Appendix P for more detailed information.
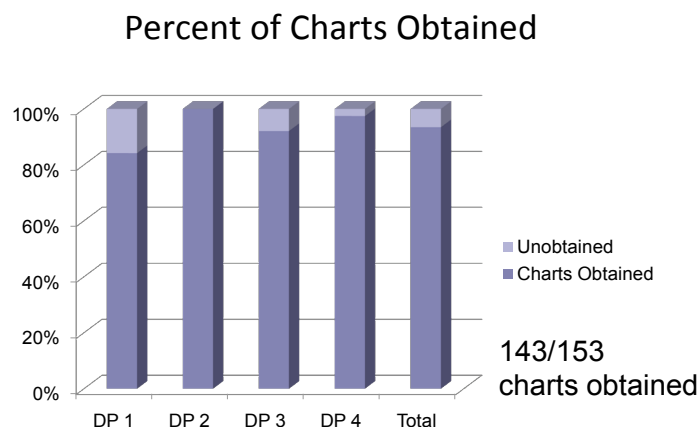
Figure 1. Percent of Charts Obtained

2. Available chart components

Critical chart components: There were several items that were considered critical to the adjudication process. These included copies of discharge summaries, copies of EKGs, and copies of laboratory results including cardiac biomarkers. As summarized in Figure 2, rates of retrieval for these critical items were over 85% across all Data Partners.

Availability of Critical Chart Components
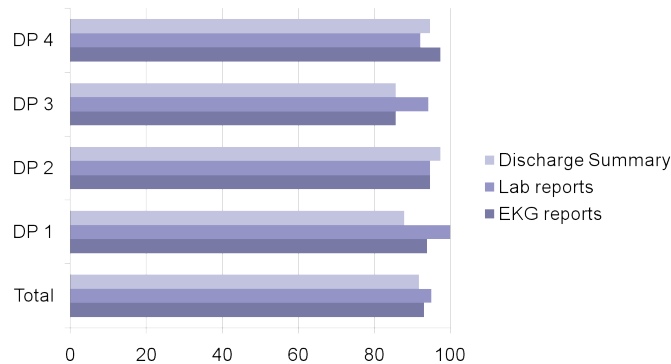
Figure 2. Availability of critical chart components

Additional chart components: Certain other chart components provided extremely important information that could be used to inform and strengthen the decisions of the adjudicators; however, this information was not expected to be present in each hospital record. These components included consult notes from cardiologists as well as reports of cardiac tests and procedures. Since not every patient diagnosed with AMI undergoes each of these tests or procedures (for example, not every AMI patient undergoes cardiac catheterization) these are items that varied by patient. In addition, the team expected to find some variation from hospital to hospital since not every hospital offers access to every test or procedure (e.g., cardiac bypass surgery). As expected, there was variability in the extent to which such information was available (Figure 3).

Availability of Cardiac-Specific Chart Components
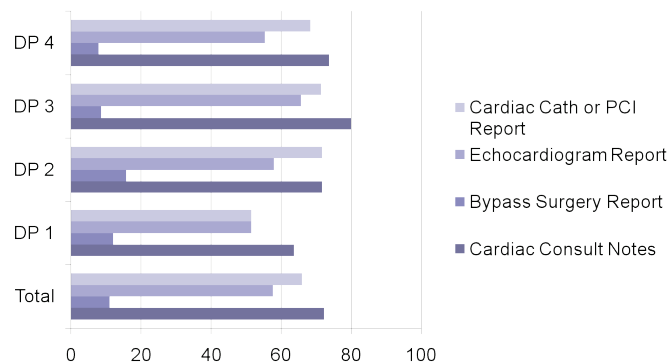
Figure 3. Availability of chart components including cardiac tests and procedures and cardiology consult notes.

3. Chart size

There was a large amount of variability in the average amount of chart materials forwarded by the Data Partners (measured by number of pages). Larger amounts of chart materials led to slower abstraction and likely required a greater expenditure of resources on the part of the Data Partner (time and resources spent copying and redacting).

Average Size of Chart (number of pages)
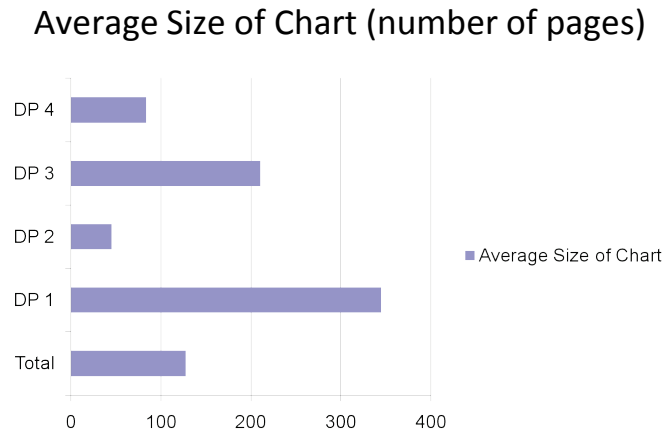
Figure 4. Average Size of Chart (Number of pages)

B. ABSTRACTION AND ADJUDICATION RESULTS

Of the 143 cases abstracted, cardiologist adjudicators determined that 123 cases were either definite or probable AMIs ("AMI+"). There were 20 cases that were judged not to be consistent with a definite or probable AMI ("AMI-"), either because one or both cardiologists felt that there was insufficient information available to confirm the presence of an AMI (14 cases), or because both cardiologists agreed that there was sufficient information available to indicate that the case was not an AMI (6 cases).

1. Positive predictive value of algorithm

Overall the PPV was 86.0% (95% confidence interval, 79.4% to 90.8%). This overall value is somewhat lower than the experience reported in prior studies and this will be discussed below in the summary section.[6-20]

The most common reason given by the cardiologists for there being insufficient information available to make a determination was lack of cardiac biomarkers; in ten cases, cardiologists stated that biomarkers were either entirely missing, incomplete with only a single value provided, or missing necessary reference levels. Other reasons included inadequate EKG data, including poor quality of copies (7 cases) or inadequate information on ischemic symptoms (7 cases). In a number of these cases, more than one deficiency was specified.

As summarized in Table 1 below, PPVs did vary across the Data Partners; PPVs ranged from 76.3% to 94.3%.

Table 1. Calculated PPV by Data Partner with 95% confidence intervals

Data Partner	AMI+	AMI-	Total # of Charts	PPV (%)	95 % Confidence Interval
DP1	26	6	32	81.3	64.7, 91.1
DP2	29	9	38	76.3	60.8, 87.0
DP3	33	2	35	94.3	81.4, 98.4
DP4	35	3	38	92.1	79.2, 97.3
OVERALL	123	20	143	86.0	79.4, 90.8

The PPV was lower for the group of patients aged 75 years and older (79.2%, 95% CI 66.5% to 88.0%) as compared to those under 75 (94.6%, 95% CI 86.9% to 97.9%). The PPV was higher for men (93.4%, 95% CI 85.5% to 97.2%) than for women (77.6%, 95% CI 66.3% to 85.9%) (see Table 2). When we analyzed PPV for men and women stratified by age, we found that there was little difference in PPV between men and women under age 75 (PPV for men 95.6%, 95% CI 85.2% to 98.8%, vs women 93.1%, 95% CI 78.0% to 98.1%) and that the difference between sexes was largely driven by differences among men and women aged 75 and older (PPV for men 88.5%, 95% CI 71.0% to 96.0%, vs women 77.6%, 95% CI 66.3% to 85.9%).

Table 2. Calculated PPV by age and gender with 95% confidence intervals

Characteristic	AMI+	AMI-	Total # of Charts	PPV (%)	95 % Confidence Interval
AGE <75	70	4	74	94.6	86.9 to 97.9
AGE 75+	42	11	53	79.2	66.5 to 88.0
MALE	71	5	76	93.4	88.5 to 97.2
<75	43	2	45	95.6	85.2 to 98.8
75+	23	3	26	88.5	71.0 to 96.0
UNAVAILABLE	5	0	5	100	
FEMALE	52	15	67	77.6	63.3 to 85.9
<75	27	2	29	93.1	78.0 to 98.1
75+	19	8	27	70.4	51.5 to 84.1
UNAVAILABLE	6	5	11	54.5	28.0 to 78.7

V. SUMMARY AND CONCLUSIONS

The AMI Validation project has established a process for validating medical outcomes within Mini-Sentinel that can serve as a model for future surveillance validation activities. The project has provided important insights into the challenges inherent in conducting HOI validation efforts. Key issues identified include: (1) the need to determine the scope of HOI definitions (broad vs more focused); (2) the need for early assessment regarding centralized vs distributed approaches to chart abstraction; and (3) the need to have established policies and approaches to maintaining patient privacy and addressing IRB issues. It will be important for future validation projects to anticipate between-hospital differences in laboratory reference standards and between-hospital variations in how these data are presented to the adjudicators.

The overall PPV determined in this project is somewhat lower than the experience reported in prior studies.[6-20] Many of these older studies did not employ the universal definition of myocardial infarction, and did not consider the evolving consensus regarding troponin levels, as they relate to this definition.

Future validation studies of AMI should consider assessing the impact of incorporating additional criteria into the algorithm (e.g., length of stay and hospital transfer criteria).

The workgroup believes that the following "lessons learned" will inform the development of best practices when conducting similar Mini-Sentinel validation activities in the future.

A. LESSONS LEARNED

1. Preparatory Stages

Workgroup: A workgroup that includes all involved parties including the FDA, the Mini-Sentinel Operations Center, and the Academic and Data Partners provided a platform for effective communication during protocol development and allowed us to identify potential challenges quickly. Regularly scheduled workgroup meetings also allowed for achieving consensus among the workgroup members with regard to project timelines, required chart components, and deliverables.

2. Chart Retrieval

Chart Request: The Operations Center provided each Data Partner with a privacy packet to disseminate to source data holders. These documents outlined the activity as public health surveillance and detailed privacy and confidentiality measures used in the activity. Data Partners distributed these documents when making the initial chart request to source data holders and the workgroup believes that this resource helped expedite the chart retrieval process.

Defining Scope: There was decision-making required surrounding what constituted a single hospitalization or a single event. Some patients were transferred to another facility in the context of care regarding a "single" event.

Privacy Packet: One Data Partner mentioned that they were asked for contract information showing that the Data Partner was a part of Mini-Sentinel. In future work, consideration should be given to adding this information to the privacy packet.

Planning for vendor and non-vendor processes: The workgroup planned for multiple chart component extraction scenarios which provided Data Partners with additional options and increased flexibility when retrieving charts.

Vendor Considerations: Some Data Partners preferred to employ vendors for chart extraction activities. This process did briefly delay the project timeline as Data Partners faced challenges in finding reasonably priced vendors. Although each chart retrieval scenario required additional resource planning, this hybrid approach made for an efficient overall chart retrieval process.

Transferring of information: The Operations Center provided Data Partners access to the Mini-Sentinel Secure Portal for transferring, managing and retrieving chart data. The Portal is a secure and efficient pathway for uploading data. The Operations Center was also able to track all data and provide abstractors access to chart extracts through this environment.

Chart size: The reasons for the high degree of variability in chart size require further exploration and are likely multi-factorial.

Chart organization: Consideration should be given in the future to assigning a set of uniform case IDs to each Data Partner to avoid the possibility of overlapping ID numbers.

3. Abstraction and Adjudication

Redaction of needed information: A well-defined protocol for redaction should be provided to every Data Partner to prevent redaction of key pieces of information necessary to facilitate the abstraction and adjudication processes. Dates of service were essential for determining whether EKGs, biomarkers or other tests corresponded to the index hospitalization or corresponded to an earlier (or later) hospitalization or healthcare encounter. In addition, certain items (e.g., EKGs and biomarkers) needed to be presented to the cardiologist adjudicators in chronological order. In cases where dates were missing, both abstractors and adjudicators were challenged unnecessarily. Use of a reference value in place of existing dates would have substantially increased the workload; requiring on-site redactors to generate reference dates would have been a substantial task. In addition, given the complexity of data necessary for the performance of the adjudications, use of a reference value for dating of services and tests would have introduced numerous opportunities for error and confusion.

VI. ACKNOWLEDGMENTS

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VIII. APPENDICES

A. APPENDIX A. MEMBERS OF THE MINI-SENTINEL ACUTE MYOCARDIAL INFARCTION (AMI) VALIDATION WORKGROUP

Name of Collaborator	Role
U.S. Food and Drug Administration	Provides FDA's input into development of AMI definition for validation and development of validation process; coordinates input of other FDA review staff and subject matter experts
Harvard Pilgrim Health Care Institute	**Mini-Sentinel Operations Center.** Creates AMI validation workgroup; provides scientific, analytic and administrative infrastructure; coordinates communication between collaborators; designs program for chart retrieval and coordinates retrieval effort.
Meyers Primary Care Institute/University of Massachusetts Medical School	**Lead Site.** Designs approach for chart identification, specifies components of chart; designs and carries out abstraction and adjudication efforts; provides cardiologists for expert adjudication.

Kaiser Permanente Center for Effectiveness and Safety Research:
   Kaiser Permanente Northern California
   Kaiser Permanente Georgia
   Kaiser Permanente Hawaii
 	
HMO Research Network:
   Group Health Cooperative
   Fallon Community Health Plan
 	
HealthCore, Inc
 	
Humana
	Data Partners. Implements computer program for identification of AMI cases; retrieves, copies, de-identifies and transmits selected healthcare data to the lead team through the Operations Center.

B. APPENDIX B. CRITICAL INFORMATION GATHERED FROM REVIEW OF PREVIOUS ACUTE MYOCARDIAL INFARCTION (AMI) VALIDATION STUDIES OF ELECTRONIC HEALTH DATA

Data Types	Algorithm Components	Algorithm Structure	Algorithm Performance Metrics
☐ Registry ☐ Hospital Administrative Data ☐ Claims data ☐ Other (Electronic health record, survey data)	☐ ICD-8, ICD-9, ICD-10 discharge codes ☐ Position of this code (primary position; first position; second position; "Most responsible diagnosis") ☐ Diagnosis-related Group (DRG) codes ☐ Other criteria: length of hospital stay (3-180 days); transfer to or from outside hospital; death during hospital stay; previous AMI in past 8 weeks	☐ Combination of codes by type (ICD-8, 9, 10, DRG) using OR vs AND ☐ Combination by position (primary only vs primary OR first vs primary OR first OR second, etc.) ☐ Combination of code with other criteria (example: ICD code AND length of stay >3 days)	☐ Sensitivity ☐ Specificity ☐ Positive predictive value (PPV)

C. APPENDIX C. ICD-9-CM CODES INCLUDED IN AMI ALGORITHM

Type of Code	Code	Description
ICD-9-CM	410.00	ACUTE MYOCARDIAL INFARCTION OF ANTEROLATERAL WALL, EPISDOE OF CARE UNSPECIFIED
ICD-9-CM	410.01	ACUTE MYOCARDIAL INFARCTION OF ANTEROLATERAL WALL, INITIAL EPISODE OF CARE
ICD-9-CM	410.10	ACUTE MYOCARDIAL INFARCTION OF OTHER ANTERIOR WALL, EPISODE OF CARE UNSPECIFIED
ICD-9-CM	410.11	ACUTE MYOCARDIAL INFARCTION OF OTHER ANTERIOR WALL, INITIAL EPISODE OF CARE
ICD-9-CM	410.20	ACUTE MYOCARDIAL INFARCTION OF INFEROLATERAL WALL, EPISODE OF CARE UNSPECIFIED
ICD-9-CM	410.21	ACUTE MYOCARDIAL INFARCTION OF INFEROLATERAL WALL, INITIAL EPISODE OF CARE
ICD-9-CM	410.30	ACUTE MYOCARDIAL INFARCTION OF INFEROPOSTERIOR WALL, EPISODE OF CARE UNSPECIFIED
ICD-9-CM	410.31	ACUTE MYOCARDIAL INFARCTION OF INFEROPOSTERIOR WALL, INITIAL EPISODE OF CARE
ICD-9-CM	410.40	ACUTE MYOCARDIAL INFARCTION OF OTHER INFERIOR WALL, EPISODE OF CARE UNSPECIFIED
ICD-9-CM	410.41	ACUTE MYOCARDIAL INFARCTION OF OTHER INFERIOR WALL, INITIAL EPISODE OF CARE
ICD-9-CM	410.50	ACUTE MYOCARDIAL INFARCTION OF OTHER LATERAL WALL, EPISODE OF CARE UNSPECIFIED
ICD-9-CM	410.51	ACUTE MYOCARDIAL INFARCTION OF OTHER LATERAL WALL, INITIAL EPISODE OF CARE
ICD-9-CM	410.60	TRUE POSTERIOR WALL INFARCTION, EPISODE OF CARE UNSPECIFIED
ICD-9-CM	410.61	TRUE POSTERIOR WALL INFARCTION, INITIAL EPISODE OF CARE
ICD-9-CM	410.70	SUBENDOCARDIAL INFARCTION, EPISODE OF CARE UNSPECIFIED
ICD-9-CM	410.71	SUBENDOCARDIAL INFARCTION, INITIAL EPISODE OF CARE
ICD-9-CM	410.80	ACUTE MYOCARDIAL INFARCTION OF OTHER SPECIFIED SITES, EPISODE OF CARE UNSPECIFIED
ICD-9-CM	410.81	ACUTE MYOCARDIAL INFARCTION OF OTHER SPECIFIED SITES, INITIAL EPISODE OF CARE
ICD-9-CM	410.90	ACUTE MYOCARDIAL INFARCTION OF UNSPECIFIED SITE, EPISODE OF CARE UNSPECIFIED
ICD-9-CM	410.91	ACUTE MYOCARDIAL INFARCTION OF UNSPECIFIED SITE, INITIAL EPISODE OF CARE

D. APPENDIX D. ALGORITHM TO IDENTIFY PATIENTS WITH ACUTE MYOCARDIAL INFARCTION IN THE MINI-SENTINEL DISTRIBUTED DATABASE

ICD-9 hospital discharge codes (a principal or primary discharge code only) of 410.x0 and 410.x1.

If a data source does not have a diagnosis designated as principal or primary, use the first-listed discharge diagnosis.

E. APPENDIX E. EXTRACTION FORM

MINI-SENTINEL: AMI VALIDATION
DATA PARTNER EXTRACTION FORM AND CHECKLIST

This form needs to be filled out for **EACH and EVERY** case for which you seek to obtain the chart. If you are unable to obtain the chart for any reason, the question "Able to obtain chart for specified case?" should be answered "no" and the form should be forwarded along.

Case ID: _____

Medical Record Extraction Date (mm/dd/yyyy)		___ / ___ / _____
Able to obtain chart for specified case?	(0 no, 1 yes)	_____
If NO, please specify reason: _____		
Same Name	(0 no, 1 yes)	_____
Same Date	(0 no, 1 yes)	_____
Actual day of admission (+/- one day of specified date)	(0 no, 1 yes)	_____
Same Date of Birth (DOB)	(0 no, 1 yes)	_____
Sex	(1= male 2= female)	_____
Do you have the correct chart? **If NO, STOP!**	(0 no, 1 yes)	_____

ICD9 code: 410. ___ ___
       Was this code (check one):
              Principal/primary discharge code ____
              Secondary ____
              Cannot determine ____

Chart Components

a.	Admission history and physical	(0 no, 1 yes)	_____
b.	Discharge summary	(0 no, 1 yes)	_____
c.	Transfer records	(0 no, 1 yes)	_____
d.	Cardiology consult notes	(0 no, 1 yes)	_____
e.	Autopsy reports/ Death notes	(0 no, 1 yes)	_____
f.	EMT/Ambulance notes	(0 no, 1 yes)	_____
g.	Emergency Department notes	(0 no, 1 yes)	_____
h.	Copies of all 12 lead EKG's	(0 no, 1 yes)	_____
i.	Laboratory reports	(0 no, 1 yes)	_____
j.	Cardiac catheterization report	(0 no, 1 yes)	_____
k.	PCI (percutaneous coronary intervention) report	(0 no, 1 yes)	_____
l.	Cardiac bypass surgery report	(0 no, 1 yes)	_____
m.	Cardiac stress tests/nuclear stress tests/reports	(0 no, 1 yes)	_____
n.	Echocardiogram reports (all)	(0 no, 1 yes)	_____

AMI Validation Workgroup 3/21/2011

F. APPENDIX F. EXTRACTION MANUAL

Mini-Sentinel: AMI Validation

Instructions for Completing

Data Partner Extraction Form

The purpose of this extraction form is to collect data from the medical record to use in validation of discharge diagnosis codes for acute myocardial infarction (MI).

The MI may be the reason for the hospitalization or it may be that the MI occurs while the patient is hospitalized for an unrelated diagnosis. The hospital chart will be the only source used to extract data. There should be only one hospitalization per extraction.

PLEASE NOTE: The Data Partner Extraction form needs to be filled out for **EACH and EVERY** case for which you seek to obtain the chart. If you are unable to obtain the chart for any reason, the question "Able to obtain chart for specified case?" should be answered "no" and the form should be forwarded along, without additional materials. Likewise, if you determine that you do not have the correct chart for any reason, the question "Do you have the correct chart?" should be answered "no" and the form should be forwarded along, without additional materials.

Administrative Information

1. Case ID:
   An internally generated ID code that will allow the Data Partner to link back to original records but will not be identifiable beyond the Data Partner.

2. Medical Record Extraction Date:
   Date extraction was completed.

3. Able to obtain chart for specified case? If NO, please specify reason:
   If chart for specified case was obtained indicate "yes" and move to next item. If chart was not able to be obtained, the specific reason should be noted.

4. Same Name:
   Indicate "yes" if patient name is the same in the chart as derived from the administrative data. Indicate "no" if patient name is different than specified based on the administrative data.

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5. Same Date:
   This item relates to the date the patient was admitted to the hospital. If the patient was transferred from another hospital or an emergency room, the date of admission will still be that date on which the patient was admitted to the hospital. Indicate "yes" if the admission date is the same in the chart as specified in the administrative data. Indicate "no" if the admission date is different in the chart than specified in the administrative data.

6. Actual day of admission (+/- one day of specified date):
   Date specified in the administrative data must be +/- one day of date of admission in the hospital record.

7. Same Date of Birth (DOB):
   Indicate "yes" if patient DOB is the same in the chart as it is in the administrative data. Indicate "no" if patient DOB is different in the chart than it is in the administrative data.

8. Sex:
   Indicate whether patient is male or female.

9. Do you have the correct chart? If NO, STOP!:
   If chart information does not correspond with administrative data and it seems that you do not have the correct chart, indicate "no" and do not proceed to next section. PLEASE NOTE: Even if you answer "NO" to this question, the Data Partner Extraction form must be forwarded to the Coordinating Center.

10. ICD9 code:
    Fill in specified code and mark whether this code was the principal/primary discharge code OR a secondary discharge code. Check "cannot determine" if you are unable to assess whether the discharge code for AMI is principal/primary or secondary.

Chart Components

Indicate for each chart component: "0" means missing or unavailable, "1" means present and included. Please be sure to write case ID number in the upper right hand corner of all copies. All of these materials should be de-identified.

1. Admission history and physical
2. Discharge summary
3. Transfer records
4. Cardiology consult notes
5. Autopsy reports/Death notes

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6. EMT/Ambulance notes
7. Emergency Department notes
8. Copies of ALL 12 lead EKG's *(Copies of all available EKG's should be included and attached)*
9. Laboratory reports
10. Cardiac catheterization report
11. PCI (percutaneous coronary intervention) report
12. Cardiac bypass surgery report
13. Cardiac stress tests/nuclear stress tests/reports
14. Echocardiogram reports *(Copies of all available Echocardiogram reports should be included and attached)*

G. APPENDIX G. PRIVACY PACKET

HIPAA and Common Rule Compliance in the Mini-Sentinel Pilot

Authored by the Mini-Sentinel Privacy Panel:
Kristen Rosati, Barbara Evans and Deven McGraw [1]

Executive Summary

This paper addresses compliance under the Common Rule and the Health Insurance Portability and Accountability Act (HIPAA) [2] for data sources participating in Mini-Sentinel, a pilot project of the Food and Drug Administration's (FDA) Sentinel Initiative, mandated by Congress in the Food and Drug Administration Amendments Act of 2007. First, as explained below, the use of data for Mini-Sentinel is a public health activity, not research. The Director of the Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP) has determined that the Common Rule does not apply to activities conducted as part of the Sentinel Initiative. Institutions participating as data sources therefore do not need to obtain review by their Institutional Review Boards (IRBs) to participate in Mini-Sentinel or to provide data for Mini-Sentinel purposes.

Second, HIPAA applies to most data sources participating in Mini-Sentinel. The access, use, and disclosure of protected health information (PHI) for purposes of Mini-Sentinel are public health activities that may be conducted without individual authorization. Moreover, data sources may rely on documentation from the FDA regarding the legal authority of the FDA and its contractors and subcontractors (including the Mini-Sentinel Coordinating Center and its Collaborating Institutions) that they are acting as public health authorities. While data sources must comply with HIPAA's minimum necessary standard in releasing PHI for Mini-Sentinel, data sources may rely on the determination by the FDA and its contractors and subcontractors regarding what constitutes the minimum amount of information necessary for the request.

This White Paper presently does not address data source compliance with the federal Part 2 regulations governing substance abuse treatment information, or compliance with state health information confidentiality laws. It will be updated in the future to discuss those compliance issues.

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[1] This White Paper was produced by the Mini-Sentinel Privacy Panel as a general reference source and is not meant to provide legal advice to any person or entity that receives a copy of the work.

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

I. Introduction: Data Flow in the Mini-Sentinel Pilot

Consistent with its mission to protect and promote the public health, the FDA is embarking on the Sentinel Initiative to create an electronic system operating across different data environments—provider electronic health records, health plan claims databases, and other electronic health care data—to monitor medical products approved by the FDA. The Sentinel Initiative will strengthen FDA's ability to monitor the performance of medical products after approval and will improve the FDA's current medical product safety surveillance capabilities.

The creation of the Sentinel Initiative is required by the Food and Drug Administration Amendments Act of 2007 (FDAAA). Section 905 of this statute calls for HHS to develop methods to obtain access to disparate electronic health care data and to establish an active post-market risk identification and analysis system that links and analyzes healthcare data from multiple environments. The law sets a goal of access to data from 25 million patients by July 1, 2010, and 100 million patients by July 1, 2012. The law also requires FDA to work closely with partners from public, academic, and private entities.

Mini-Sentinel is a pilot project of the Sentinel Initiative intended to provide the foundational work necessary to inform and facilitate the development of a fully operational active surveillance system for monitoring the safety of FDA-regulated medical products (the Sentinel System). The Mini-Sentinel pilot is being conducted as a collaborative effort by a consortium that includes a variety of hospital systems, health plans, universities, and research institutes (called the Collaborating Institutions in this paper).[3]

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[3] The Collaborating Institutions include:
1. America's Health Insurance Plans (AHIP)
2. Brigham and Women's Hospital Division of General Medicine
3. Brigham and Women's Hospital Division of Pharmacoepidemiology & Pharmacoeconomics
4. CIGNA Healthcare
5. Cincinnati Children's Hospital Medical Center
6. Columbia University Department of Statistics
7. Critical Path Institute (C-Path)
8. Duke University School of Medicine
9. HealthCore, Inc.
10. HMO Research Network including: Group Health Research Institute (GHRI) at the University of Washington (UW); Harvard Pilgrim Health Care Institute (HPHCI); Health Partners Research Foundation; Henry Ford Health Systems; Lovelace Clinic Foundation; Marshfield Clinic Research Foundation; Meyers Primary Care Institute (Fallon)
11. Humana-Miami Health Services Research Center (HSRC)
12. Kaiser Permanente Center for Safety and Effectiveness Research (CESR) including: Northern California (KPNC); Southern California (KPSC); Colorado (KPCO); Northwest (KPNW); Georgia (KPSE); Hawaii (KPHI); Ohio (KPOhio); MidAtlantic (KPMidAtlantic)
13. Outcome Sciences, Inc. (Outcome)
14. Risk Sciences International (RSI)
15. Rutgers University Institute for Health

The objective of the Mini-Sentinel pilot is to inform and facilitate the development of the Sentinel System and carry out mandates delineated in FDAAA. Specifically, the Mini-Sentinel contract funds the development of a single Mini-Sentinel Coordinating Center with continuous access to electronic healthcare data systems, which will:

1. Provide a "laboratory" for developing and evaluating scientific methodologies that might later be used in a fully-operational Sentinel System;
2. Offer the FDA the opportunity to evaluate safety issues in existing electronic healthcare data systems; and
3. Learn more about some of the barriers and challenges, both internal and external, faced in creating a medical products safety surveillance system.

Representatives of the Mini-Sentinel Collaborating Institutions provide ongoing scientific, technical, methodologic, and governance expertise, as well as access to data, as needed to meet the requirements of the project. They participate in various capacities, including as data sources and as members of the Planning Board, the Safety Science Committee, the Cores (Data, Methods, and Protocol), and Working Groups for Task Orders and other activities.

No directly identifiable data will flow to the Mini-Sentinel Coordinating Center or to the FDA. Collaborating Institutions will maintain physical and operational control over the data. They will execute analysis programs distributed by the Coordinating Center, and provide the output of these programs to the Coordinating Center. Whenever possible, the output they share will contain only summary or aggregate information, such as counts of health plan members categorized by: 1) the presence or absence of a particular health condition; 2) exposure to a particular medication; 3) the presence or absence of a particular health outcome; and 4) age group. When person-level information is provided, it will be stripped of all directly identifiable data. For example, in order to confirm an adverse drug reaction, the Collaborating Institutions may provide clinical data about a particular individual, but this data will exclude any direct identifiers such as name and contact information.

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16. University of Alabama at Birmingham (UAB)
17. University of Illinois at Chicago (UIC)
18. University of Iowa, College of Public Health
19. University of Pennsylvania School of Medicine
20. Vanderbilt University School of Medicine
21. Weill Cornell Medical College
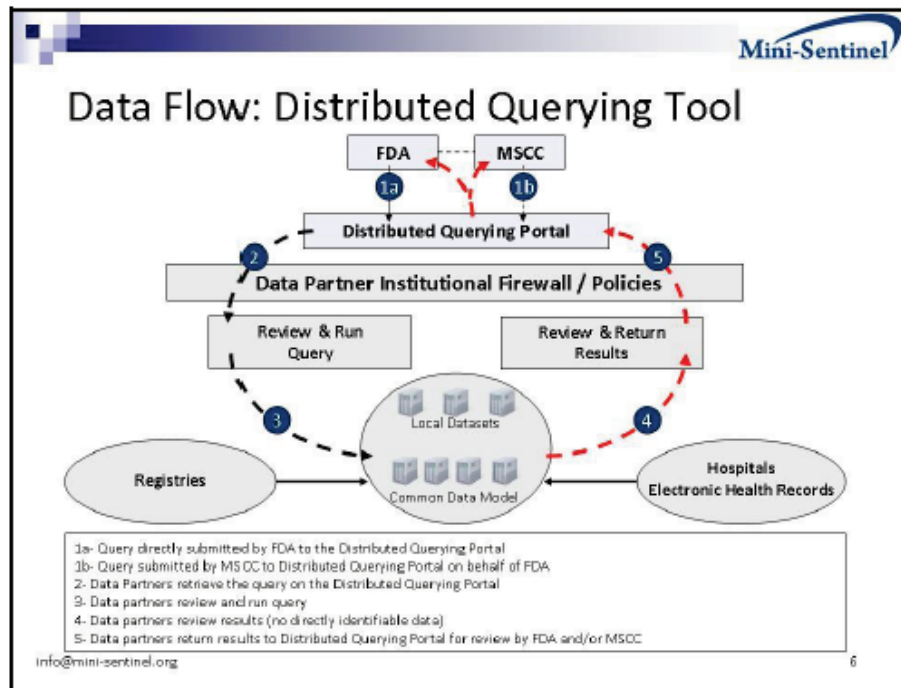
Figure 2

It is possible that some of the aggregate data flowing to the Coordinating Center will technically be "protected health information" (PHI) under HIPAA because the information reported may include dates of service or geographic codes (data elements that are listed as HIPAA "identifiers"), or because the information may represent "small cells" in which the diagnosis is sufficiently unique to be able to identify an individual if paired with other available information. Because data that is classified as PHI may flow to the Coordinating Center, we evaluate below whether this would comply with the HIPAA Privacy Rule.[4]

Moreover, it is possible that fully-identifiable PHI may flow from HIPAA covered entities to the Collaborating Institutions to confirm the validity of adverse event drug safety signals. For example, a Collaborating Institution might ask for portions of the medical record from a treating health care provider to determine if the drug in question was administered before or after the adverse clinical event occurred, or to determine whether other patient conditions may have resulted in the adverse clinical event observed. Another example involves state immunization registries: to evaluate the safety of immunizations, Collaborating Institutions may seek information from immunization registries regarding whether individuals

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[4] 45 C.F.R. Part 160 and Part 164, Subpart E.

have received certain immunizations. Because PHI may flow to the Collaborating Institutions, we evaluate below whether this would comply with the HIPAA Privacy Rule.[5]

This paper first addresses Common Rule compliance for any data source supplying information to the FDA, the Mini-Sentinel Coordinating Center, or the Collaborating Institutions, for the purpose of the Mini-Sentinel pilot.

II. Common Rule Compliance

The Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP) has concluded that activities related to the Sentinel Initiative are not covered by 45 CFR part 46 (the "Common Rule"). This means that cooperation in responding to Sentinel queries does <u>not</u> require review by an Institutional Review Board (IRB). On January 19, 2010, Jerry Menikoff, Director of the OHRP, wrote a letter to Rachel Behrman, then Acting Associate Director of Medical Policy, Center for Drug Evaluation and Research at the FDA, explaining that OHRP "has determined that the regulations this office administers (45 CFR part 46) do not apply to the activities that are included in the [FDA] Sentinel Initiative." (See Exhibit 1.) Dr. Behrman then wrote on April 2, 2010, to Dr. Richard Platt at Harvard Pilgrim Health Care (the Mini-Sentinel's prime contractor managing the Coordinating Center), providing Dr. Menikoff's letter and concluding that the OHRP's "assessment applies to the work being conducted by [Harvard Pilgrim Health Care] and its subcontractors under contract number HHSF2232009100061, as the purpose of this contract is to carry out Sentinel Initiative activities that are included in the [FDA] Sentinel Initiative." (See Exhibit 2.) Thus, disclosure of information for Mini-Sentinel purposes is not subject to the Common Rule. This means that data sources providing information for Mini-Sentinel purposes are not required by federal regulation to obtain approval of their IRBs for participation in Mini-Sentinel, and are not required to obtain a determination from their IRBs that these activities are "exempt."

III. HIPAA Compliance

A. Disclosures of Protected Health Information in Support of Mini-Sentinel Are for Public Health Activities under HIPAA

The provision of data to the FDA, the Mini-Sentinel Coordinating Center, and to the Collaborating Institutions is to support a public health activity that is permitted under the HIPAA Privacy Rule without patient authorization. The HIPAA Privacy Rule permits covered entities to disclose PHI for a variety of public health purposes, including to:

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[5] In this version of the White Paper we do not address compliance with state health information confidentiality laws, such as state laws governing permissible disclosures by their immunization registries.

> [A] public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability, including, but not limited to, the reporting of disease, injury, vital events such as birth or death, and the conduct of public health surveillance, public health investigations, and public health interventions; or, at the direction of a public health authority, to an official of a foreign government agency that is acting in collaboration with a public health authority.[6]

The FDA is a "public health authority" under HIPAA, which is defined as:

> an agency or authority of the United States, a State, a territory, a political subdivision of a State or territory, or an Indian tribe, or a person or entity acting under a grant of authority from or contract with such public agency, including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its official mandate.[7]

The release of PHI to the FDA for purposes of drug safety surveillance is for the "conduct of public health surveillance" purposes, as contemplated by the rule.[8]

Moreover, the Mini-Sentinel Coordinating Center and its subcontractors (the Collaborating Institutions) are functioning as "public health authorities," as well, because they are acting under contract with or under a grant of authority from the FDA. The Mini-Sentinel Coordinating Center is performing its functions under contract with the FDA. Moreover, even though the Collaborating Institutions do not have a direct contract with the FDA, FDA has issued a letter to the Mini-Sentinel Coordinating Center explaining that both the Mini-Sentinel Coordinating Center and its subcontractors are acting under a grant of authority from the FDA. (See Exhibit 3.) Thus, data sources may release PHI requested by the Mini-Sentinel Coordinating Center and the Collaborating Institutions as "public health authorities" for the purpose of the Mini-Sentinel pilot medical product safety surveillance queries.[9]

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[6] 45 C.F.R. §164.512(b)(1)(i).

[7] 45 C.F.R. §164.501 (emphasis added).

[8] "[T]he Privacy Rule specifically permits covered entities (such as pharmacists, physicians or hospitals) to report adverse events and other information related to the quality, effectiveness and safety of FDA-regulated products both to the manufacturers and directly to FDA." *See* http://www.fda.gov/medwAtch/hipaa.htm (citing HHS Office for Civil Rights Guidance Explaining Significant Aspects of the Privacy Rule at page 28).

[9] The internal use of PHI by the Collaborating Institution would similarly be permitted under HIPAA. . . . . *See* Barbara J. Evans, Authority of the Food and Drug Administration to Require Data Access and Control Use Rights in the Sentinel Data Network, 65 Food & Drug Law Journal 67-112 (2010);

Where a disclosure of PHI is to a public health authority, the HIPAA Privacy Rule *does not* require the covered entity to have an IRB or Privacy Board determine whether the covered entity may make the disclosure.

B.   The Mini-Sentinel Pilot Documentation Provides Required Verification of Identity and Authority to Request PHI

To disclose PHI to the FDA or an entity acting under a contract or other grant of authority from the FDA, data sources must confirm the recipient's identity and that the recipient has the legal authority to request the PHI.[10] A covered entity is entitled to rely on written confirmation on FDA letterhead that the Mini-Sentinel Coordinating Center and the Collaborating Institutions are acting on behalf of the FDA, and that they have the legal authority to request PHI for the Mini-Sentinel pilot.[11] FDA has issued a letter to the Mini-Sentinel Coordinating Center explaining that both the Mini-Sentinel Coordinating Center and the Collaborating Institutions are acting under a grant of authority from the FDA, pursuant to the legal authority provided by the FDAAA. (See Exhibit 3.)

In other words, the data sources are not expected to make their own independent inquiry into whether queries from the FDA, the Mini-Sentinel Coordinating Center or the Collaborating Institutions serve a legally authorized public health purpose.

C.   A Data Use Agreement Is Not Required for Disclosure to a Public Health Authority

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[10] 45 C.F.R. § 164.514(h)(1)(i).
[11] 45 C.F.R. § 164.514(h)(2)(ii)(C) (allowing a covered entity, when making disclosure to a person acting on behalf of a public official, to rely on "a written statement on appropriate governmental letterhead that the person is acting under the government's authority or other evidence or documentation of the agency, such as a contract for services … that establishes that the person is acting on behalf of the public official"; 45 C.F.R. § 164.514(h)(2)(iii)(A) (permitting a covered entity to rely on the written statement of a public agency regarding the legal authority under which it is requesting PHI, or an oral statement if a written statement is impracticable).

The Preamble to the Privacy Rule explained further: "For most disclosures, verifying the authority for the request means taking reasonable steps to verify that the request is lawful under this regulation…. Where the person requesting the protected information is a public official, covered entities must verify the identity of the requester by examination of reasonable evidence, such as a written statement of identity on agency letterhead, an identification badge, or similar proof of official status. . . . . Similarly, covered entities are required to verify the legal authority supporting the request by examination of reasonable evidence, such as a written request provided on agency letterhead that describes the legal authority for requesting the release. . . . . In some circumstances, a person or entity acting on behalf of a government agency may make a request for disclosure of protected health information under these subsections. . . . . For example, public health agencies may contract with a nonprofit agency to collect and analyze certain data. . . . . In such cases, the covered entity is required to verify the requestor's identity and authority through examination of reasonable documentation that the requestor is acting on behalf of a government agency. . . . . Reasonable evidence includes a written request provided on agency letterhead that describes the legal authority for requesting the release and states that the person or entity is acting under the agency or authority." 65 Fed. Reg. at 82547 (emphasis added).

Where the disclosure of PHI is to a public health authority, the HIPAA Privacy Rule does not require the recipient to sign a Data Use Agreement. The HIPAA Privacy Rule does permit a covered entity to release a "Limited Data Set" (partially de-identified data) for public health, research and health care operations purposes, as long as the covered entity first obtains a Data Use Agreement with the recipient of the Limited Data Set.[12] This rule permits the release of a Limited Data Set to entities that are not "public health authorities" under HIPAA, but that are using it for public health purposes. However, if the disclosure of PHI is to a "public health authority," that disclosure does not need to be limited to a Limited Data Set nor requires a Data Use Agreement. Rather, covered entities may release fully-identifiable PHI to public health authorities.[13]

D. The Mini-Sentinel Pilot Documentation Meets Data Source Obligations to Comply with the Minimum Necessary Standard

HIPAA covered entities must observe the "minimum necessary standard" in releasing PHI for public health purposes. This simply means that a covered entity must make reasonable efforts to limit the information to the minimum amount of information that is necessary to accomplish the intended purpose of the disclosure,[14] with some limited exceptions not relevant here.[15] A covered entity may not disclose the entire medical record unless there is a specific justification for doing so.[16]

Under the HIPAA Privacy Rule, a covered entity may rely on a public health authority's determination that the data requested are the minimum necessary data that the agency needs to fulfill the purpose of its request.[17] When FDA (or the Coordinating Center or Collaborating Institutions acting on behalf of FDA) sends a query to a covered entity, Mini-Sentinel policies require the request to be limited to what is required to evaluate the drug safety issue. Covered entities thus may rely on these public health authority requests as being limited to the minimum amount of PHI necessary for the Mini-Sentinel activities.

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[12] 45 C.F.R. § 164.514(d).

[13] 45 C.F.R. § 164.512(b).

[14] 45 C.F.R. § 164.502(b)(1). . . . .

[15] 45 C.F.R. § 164.502(b)(2).

[16] 45 C.F.R. § 164.514(d)(5). . . . .

[17] See 45 C.F.R. § 164.514(d)(3)(iii) ("A covered entity may rely, if such reliance is reasonable under the circumstances, on a requested disclosure as the minimum necessary for the stated purpose when: (A) Making disclosures to public officials that are permitted under § 164.512, if the public official represents that the information requested is the minimum necessary for the stated purpose." While §13405(b) of the Health Information Technology for Economic and Clinical Health Act (the HITECH Act), codified at 42 U.S.C. § 17935, contains a provision that requires covered entities to determine what is the minimum amount of PHI for a disclosure, the proposed amendments to the HIPAA Privacy Rule to implement the HITECH Act do not modify a covered entity's ability to rely on minimum necessary representations by public officials. . . . . (See Notice of Proposed Rule Making, "Modifications to the HIPAA Privacy, Security, and Enforcement Rules under the [HITECH] Act," at http://www.ofr.gov/OFRUpload/OFRData/2010-16718_PI.pdf, scheduled for publication in the Federal Register on July 14th.)

IV.   Conclusion

Data source participation in the Mini-Sentinel pilot complies both with the Common Rule and HIPAA. OHRP has determined that Sentinel activities are not governed by the Common Rule. Moreover, the disclosure of PHI to the FDA, the Mini-Sentinel Coordinating Center and the Collaborating Institutions is disclosure of PHI to "public health authorities," and thus does not require individual authorization or IRB approval.

Exhibit 1

DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
Rockville, Maryland 20852

JAN 1 9 2010

Rachel E. Behrman, M.D., M.P.H.
Acting Associate Director of Medical Policy
Center for Drug Evaluation and Research
Food and Drug Administration
Bldg 22, Room 4208
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

Dear Dr. Behrman:

The Office for Human Research Protections has determined that the regulations this office administers (45 CFR part 46) do not apply to the activities that are included in the Food and Drug Administration's Sentinel Initiative.

Do not hesitate to contact us if we can be of any further assistance.

Sincerely,

Jerry Menikoff, M.D., J.D.
Director
Office for Human Research Protections

cc: Joanne Less, FDA

Exhibit 2

DEPARTMENT OF HEALTH & HUMAN SERVICES   Public Health Service

Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993

April 2, 2010

Dr. Richard Platt
Professor and Chair of the Department of Ambulatory Care and Prevention
Harvard Medical School and Harvard Pilgrim Health Care
133 Brookline Ave
Boston, MA 02215

Dear Dr. Platt:

The attached letter from the Office for Human Research Protections states: "The Office for Human Research Protections has determined that the regulations this office administers (45 CFR Part 46) do not apply to the activities that are included in the Food and Drug Administration's Sentinel Initiative."

This assessment applies to the work being conducted by you and your subcontractors under contract number HHSF223200910006I, as the purpose of this contract is to carry out activities that are included in the Food and Drug Administration's Sentinel Initiative.

Please let me know if you have any questions.

Rachel E. Behrman, MD, MPH
Sentinel Initiative, Executive Sponsor

Exhibit 3

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993

July 19, 2010

Dr. Richard Platt

Professor and Chair of the Department of Ambulatory Care and Prevention

Harvard Medical School and Harvard Pilgrim Health Care

133 Brookline Ave

Boston, MA 02215

Re: HIPAA Compliance for Data Sources Participating in the Mini-Sentinel Pilot Project

Dear Dr. Platt:

This letter affirms that the activities performed by the Mini-Sentinel Coordinating Center (MSCC) and its Collaborating Institutions,[1] in fulfillment of contract number HHS F223200910006I, are

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[1]   The Collaborating Institutions include:
1. America's Health Insurance Plans (AHIP)
2. Brigham and Women's Hospital Division of General Medicine
3. Brigham and Women's Hospital Division of Pharmacoepidemiology & Pharmacoeconomics
4. CIGNA Healthcare
5. Cincinnati Children's Hospital Medical Center
6. Columbia University Department of Statistics
7. Critical Path Institute (C-Path)
8. Duke University School of Medicine
9. HealthCore, Inc.
10. HMO Research Network including: Group Health Research Institute (GHRI) at the University of Washington (UW); Harvard Pilgrim Health Care Institute (HPHCI); Health Partners Research Foundation; Henry Ford Health Systems; Lovelace Clinic Foundation; Marshfield Clinic Research Foundation; Meyers Primary Care Institute (Fallon)
11. Humana-Miami Health Services Research Center (HSRC)
12. Kaiser Permanente Center for Safety and Effectiveness Research (CESR) including: Northern California (KPNC); Southern California (KPSC); Colorado (KPCO); Northwest (KPNW); Georgia (KPSE); Hawaii (KPHI); Ohio (KPOhio); MidAtlantic (KPMidAtlantic)
13. Outcome Sciences, Inc. (Outcome)
14. Risk Sciences International (RSI)
15. Rutgers University Institute for Health
16. University of Alabama at Birmingham (UAB)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993

public health activities for which HIPAA permits covered entities to disclose Protected Health Information (PHI) without individual authorization and without the need to obtain approval by or waiver of HIPAA authorization from an Institutional Review Board or Privacy Board.

The HIPAA Privacy Rule, at 45 C.F.R. § 164.512(b)(1)(i), permits covered entities to disclose PHI to a public health authority. The FDA is a public health authority, and has legal authority under Section 905 of the Food and Drug Administration Amendments Act of 2007 (Pub. L. No. 110-85) to conduct activities related to the project entitled, *Detection and Analysis of Adverse Events related to Regulated Products in Automated Healthcare Data. Efforts to Develop the Sentinel Initiative* (the Mini-Sentinel pilot project).

Under 45 C.F.R. § 164.501, a "public health authority" includes the FDA and "a person or entity acting under a grant of authority from or contract with" the FDA. Harvard Pilgrim Health Care is acting under the above-referenced contract with FDA to operate the MSCC. The Collaborating Institutions are under subcontract to Harvard Pilgrim Health Care to conduct activities in furtherance of FDA's Mini-Sentinel pilot project. As such, MSCC and the Collaborating Institutions are all acting under a grant of authority from FDA and have the status of public health authorities under the HIPAA Privacy Rule for purposes of carrying out their responsibilities under the Mini-Sentinel pilot project.

HIPAA covered entities are required to verify that a person requesting PHI for public health purposes is a public health authority. For this purpose, HIPAA covered entities are entitled to rely on a written statement on appropriate government letterhead that the person is acting under the government's authority (see 45 C.F.R. § 164.514(h)(2)(ii)(C)). This letter serves to provide the necessary written statement of authority to the MSCC and the Collaborating Institutions.

The HIPAA Privacy Rule also requires covered entities to comply with the minimum necessary rule at 45 C.F.R. § 164.502, but permits covered entities to rely on representations by a public health authority that it is requesting only the minimum amount of PHI necessary to carry out its public health mission (see 45 C.F.R. 164.514(d)(3)(iii)(A)). The Mini-Sentinel pilot project policies require MSCC and the Collaborating Institutions to request only the minimum necessary information that is required for purposes of carrying out their responsibilities. Thus, HIPAA covered entities may determine that requests from the MSCC and its Collaborating Institutions meet the minimum necessary standard.

Finally, because disclosures of PHI for the Mini-Sentinel pilot project are for public health activities, it is not necessary for HIPAA covered entities to obtain approval by their IRBs or

17. University of Illinois at Chicago (UIC)
18. University of Iowa, College of Public Health
19. University of Pennsylvania School of Medicine
20. Vanderbilt University School of Medicine
21. Weill Cornell Medical College

H. APPENDIX H. LETTER TO PROVIDERS FROM DATA PARTNERS

<DATE>

<PROVIDER NAME>

<PROVIDER ADDRESS>

Re: Medical Records Request for FDA Drug Safety Monitoring System

We are contacting you regarding a project to facilitate the development of a fully operational drug safety system for monitoring FDA-regulated medical products. <DATA PARTNER> is collaborating on this endeavor, Mini-Sentinel, with the Department of Population Medicine, Harvard Medical School/Harvard Pilgrim Healthcare Institute, and the FDA.

This pilot has been designed in response to a Congressional mandate to monitor drug safety and your cooperation is key to successfully addressing this FDA priority public health initiative. In order to conduct this project, we require review of medical records for some of your patients diagnosed with Acute Myocardial Infarction.

We request that you: 1) allow us access to the relevant records for the attached list of patients; 2) obtain the relevant records for the attached list of patients and redact the individually identifiable health information and then send a copy of the record to us; or 3) send a copy of the record to <VENDOR>, a redaction service provider contracted by us, which will send the information to us after it has been redacted.

Enclosed are two letters from the FDA and Office of Human Research Protections identifying this as a priority public health surveillance activity that does not require authorization from you Institutional Review Board (IRB) or Privacy Board.

If you have any questions, please contact <NAME> at (###) ###-####. She/He is our leading research manager on this record review process and will be your key contact.
We greatly appreciate your time and assistance with this important public health initiative.

Sincerely,

Name
Title

I. APPENDIX I. POSSIBLE SCENARIOS FOR CHART RETRIEVAL AND DETAILED STEPS FOR CHART REDACTION AND DATA TRANSMISSION ENVISIONED IN THE MINI-SENTINEL ACUTE MYOCARDIAL INFARCTION (AMI) VALIDATION ACTIVITY

Medical Record Information Flow Chart for AMI Validation Project 10.7.10
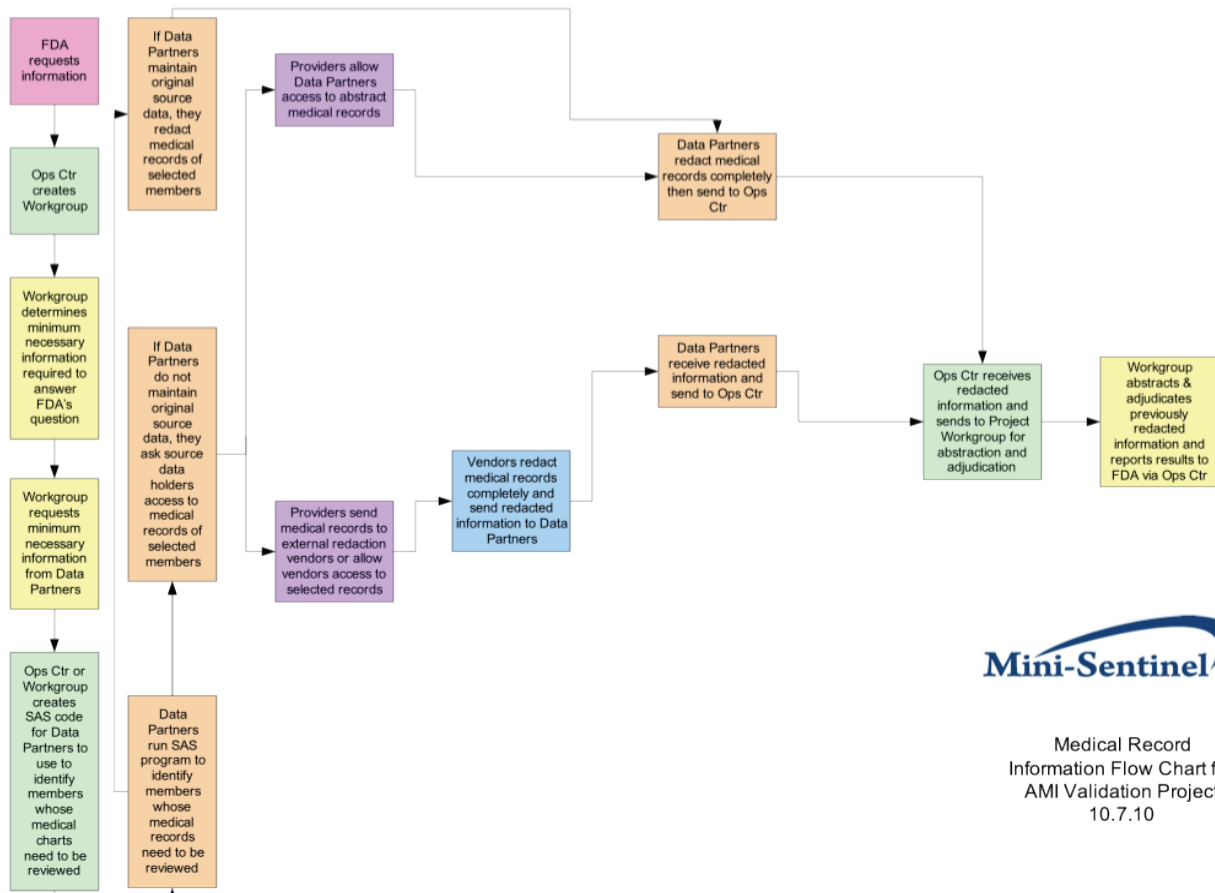
J. APPENDIX J. PROTOCOL DEVIATION CORRECTION PROCESS

Protocol Deviation Correction Process
2.11.11
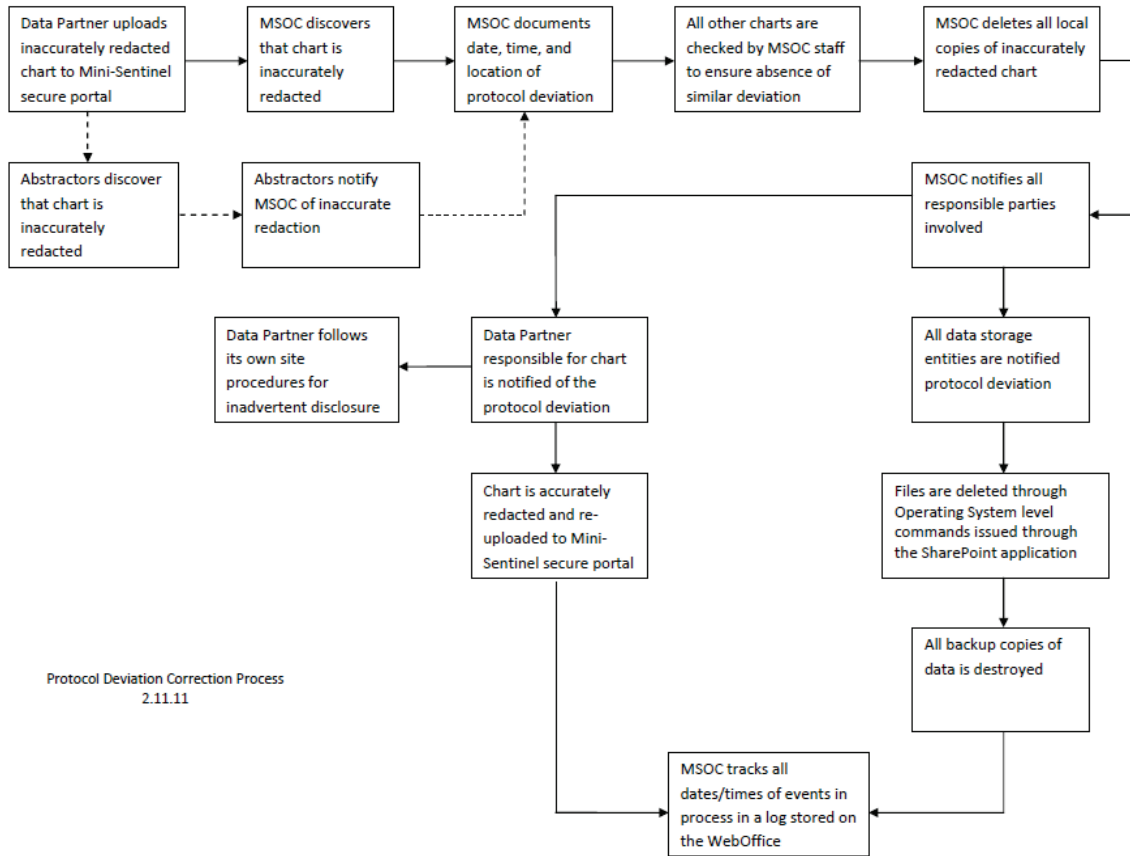
K. APPENDIX K. SAMPLE FREQUENTLY ASKED QUESTIONS SENT BY DATA PARTNERS TO PROVIDER SITES

Sample Frequently Asked Questions sent by Data Partners to provider sites

Q: Who is Data Partner?
A: Variable

Q: Who is the Vendor for chart abstraction/extraction?
A: Variable

Q: How were the providers selected to participate in this study?
A: Mini-Sentinel AMI Validation Workgroup developed an algorithm to identify potential cases of AMI. A SAS program based on this algorithm was distributed to participating Data Partners which was then run on their local Mini-Sentinel Distributed Database. Mini-Sentinel uses a distributed data approach in which Data Partners maintain physical and operational control over electronic data in their existing environments. Data Partners executed the standardized program provided by the Operations Center and then shared the output of these programs, with the Operations Center. Cases and corresponding provider sites were identified through these data outputs.

Q: Where will the abstracted data go?
A: The abstracted data was sent to the Mini-Sentinel Operations Center via the Mini-Sentinel secure portal. The portal consists of a set of Virtual Machines, two firewall zones, and dedicated storage volumes. Security of this portal is managed within the folder structure of the site; private folders are accessible only to specified members within each Data Partner site and authorized Operations Center staff.

Q: How can I contact the Data Partner directly?
A: Variable based on Data Partner

L. APPENDIX L. DATA PARTNER SURVEY

Secondary Data Partner Query Form
3.3.11

A. **OVERALL PROCESS MANAGEMENT**
1. Who was in charge of managing chart retrieval process at your site?
2. Did this staff member participate in the biweekly workgroup calls?
   a. If no, then which team member did?
   b. How was information from the workgroup meetings disseminated?

B. **CHART RETREIVAL**
1. Did the Data Partner electronically or physically retrieve data?
2. Was a request sent to the provider and the provider staff returned charts?
   a. If yes, what instructions and training were providers given?
   b. Did this create delays? Why?
3. Were sites instructed to return only chart components listed on the extraction form?

C. **CHART REDACTIONS**
1. Who performed the chart redactions?
2. Did the redactor receive training or instructions?
   a. If so, what was done?
   b. What items were the redactors instructed to redact?
3. Did any sites do redaction?
   a. If so, were they given training or instructions?

D. **CHART UPLOAD**
1. Who uploaded charts to MSOC portal?
2. Was the data checked prior to upload?

E. **VENDOR**
1. If your site used a vendor, how was the vendor team managed?
2. What was the chart request process?
3. What instructions and training was given to vendors?

F. **PROVIDER SITES PROCEDURES**
1. Who at each provider site was contacted with chart request?
2. Did sites charge for charts?
   a. If so, what were the charges?
3. Did providers have limits on the number of charts or the number of pages per chart?

G. **OTHER COMMENTS**

M. APPENDIX M. ABSTRACTION FORM

Case ID: _____

Mini-Sentinel: AMI Validation
Acute Myocardial Infarction
Abstraction Form

Instructions: This form is for use in validation of discharge diagnosis codes for acute myocardial infarction. See Instruction Manual for detailed guidelines for each form item.

Abstractor's Initials ☐☐☐

Abstraction Date ☐☐ / ☐☐ / ☐☐

Data Partner Name ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

AMI Validation Workgroup

Case ID: _____

Section 1: General information

1. Date of admission: __ __ / __ __ / __ __ __ __

2. Date of discharge: __ __ / __ __ / __ __ __ __

3. Was this patient transferred <u>from</u> another hospital?   YES__   NO__

4. Race/Ethnicity (check all that apply):
     WHITE___
     BLACK___
     NATIVE AMERICAN____
     ASIAN___
     HISPANIC___
     NON-HISPANIC___
     OTHER___
     UNAVAILABLE/UNKNOWN__

5. Age: ____
     UNAVAILABLE__

6. Gender:
     MALE _____   FEMALE_____   UNAVAILABLE__

Section 2: Medical history

7. Was there a documented acute episode of symptoms consistent with cardiac ischemia? (Symptoms include: chest pain/pressure/tightness/burning, left arm pain, jaw or neck pain, SOB/dyspnea, sweating/diaphoresis, nausea/vomiting.)

YES__   NO__   UNKNOWN__

8. Is there evidence in the patient records of a prior myocardial infarction?

YES__   NO__

        8a. If YES, was the patient discharged within the past 10 days?

                YES__   NO__   UNAVAILABLE__

AMI Validation Workgroup

Section 3: Biomarkers

Biomarkers Laboratory Standards:

Instructions: if only one value given, such as <0.03, include this in Upper reference limit column (with a
< or <=sign.) Units: 1= ng/mL; 2=Units/L; 3=μg/L; 4=Other

Biomarker	Upper reference limit (URL)	Indeterminant range (if given)	Abnormal (consistent with necrosis)	Units	99th percentile of the URL*
9. Total CK (CPK)					
10. CK-MB					
11. Troponin I					
12. Troponin T					
13. Troponin (other):_____					
14. Troponin (other):_____					

*If lab or chart provides a 99th percentile of the URL for Troponin I or T, please enter.

Biomarkers Measurements:

	15. Initial levels		16.01. Subsequent levels	
Total CK	a. _ _ _ _ _	Date: _ _/_ _/_ _ Time _ _:_ _	a. _ _ _ _ _	Date: _ _/_ _/_ _ Time _ _:_ _
CK-MB	b. _ _ _ _ _	Date: _ _/_ _/_ _ Time _ _:_ _	b. _ _ _ _ _	Date: _ _/_ _/_ _ Time _ _:_ _
Troponin I	c. _ _ _ _ _	Date: _ _/_ _/_ _ Time _ _:_ _	c. _ _ _ _ _	Date: _ _/_ _/_ _ Time _ _:_ _
Troponin T	d. _ _ _ _ _	Date: _ _/_ _/_ _ Time _ _:_ _	d. _ _ _ _ _	Date: _ _/_ _/_ _ Time _ _:_ _
Troponin (other):_____	e. _ _ _ _ _	Date: _ _/_ _/_ _ Time _ _:_ _	e. _ _ _ _ _	Date: _ _/_ _/_ _ Time _ _:_ _
Troponin (other):_____	f. _ _ _ _ _	Date: _ _/_ _/_ _ Time _ _:_ _	f. _ _ _ _ _	Date: _ _/_ _/_ _ Time _ _:_ _

AMI Validation Workgroup

	16.02. Subsequent levels		16.03. Subsequent levels	
Total CK	a. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _	a. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _
CK-MB	b. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _	b. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _
Troponin I	c. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _	c. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _
Troponin T	d. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _	d. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _
Troponin (other):_____	e. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _	e. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _
Troponin (other):_____	f. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _	f. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _
	16.04. Subsequent levels		16.05. Subsequent levels	
Total CK	a. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _	a. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _
CK-MB	b. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _	b. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _
Troponin I	c. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _	c. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _
Troponin T	d. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _	d. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _
Troponin (other):_____	e. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _	e. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _
Troponin (other):_____	f. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _	f. _ _ _ _	Date: _ _/_ _/_ _ Time_ _:_ _

AMI Validation Workgroup

SUPPLEMENTAL SECTION: PREHOSPITAL BIOMARKERS
Biomarkers Laboratory Standards:

Instructions: if only one value given, such as <0.03, include this in Upper reference limit column (with a < or <=sign.) Units: 1= ng/mL; 2=Units/L; 3=μg/L; 4=Other

Biomarker	Upper reference limit (URL)	Indeterminant range (if given)	Abnormal (consistent with necrosis)	Units	99th percentile of the URL*
S1. Total CK (CPK)					
S2. CK-MB					
S3. Troponin I					
S4. Troponin T					
S5. Troponin (other) _____					
S6. Troponin (other) _____					

	S7. First Available Levels		S7. Subsequent levels	
Total CK	a. __ __ __ __	Date: __/__/__ Time__:__	a. __ __ __ __	Date: __/__/__ Time__:__
CK-MB	b. __ __ __ __	Date: __/__/__ Time__:__	b. __ __ __ __	Date: __/__/__ Time__:__
Troponin I	c. __ __ __ __	Date: __/__/__ Time__:__	c. __ __ __ __	Date: __/__/__ Time__:__
Troponin T	d. __ __ __ __	Date: __/__/__ Time__:__	d. __ __ __ __	Date: __/__/__ Time__:__
Troponin (other):_____	e. __ __ __ __	Date: __/__/__ Time__:__	e. __ __ __ __	Date: __/__/__ Time__:__
Troponin (other):_____	f. __ __ __ __	Date: __/__/__ Time__:__	f. __ __ __ __	Date: __/__/__ Time__:__

AMI Validation Workgroup

Section 4: Electrocardiogram(s) (Attach copies of _all_ available electrocardiograms)

17. Were any 12 lead ECGs taken during this admission?

      YES__   NO__> (go to item 21)   UNKNOWN__> (go to item 21)

18. First ECG taken after arrival at the surveillance hospital:

      a. Date: __ __/__ __/__ __ __ __   b. time: __ __:__ __

19. Were there other ECGs available?

      YES__   NO__

20. Last ECG on this admission:

      a. Date: __ __/__ __/__ __ __ __   b. time: __ __:__ __

Section 5: Echocardiogram(s) (Attach copies of _all_ available echocardiogram reports)

21. Was an echocardiogram performed during this admission?

      YES__   NO__   UNKNOWN__

22. Is an echocardiogram report or interpretation available?

      YES__   NO__

Section 6: Procedures or Interventions Performed During Hospitalization

23. Was a thrombolytic agent administered?

      YES__   NO__   UNKNOWN__

24. Cardiac catheterization with or without percutaneous coronary intervention (PCI)?

      YES__ (attach copy of report)   NO__   UNKNOWN__

      a. Date: __ __/__ __/__ __ __ __

AMI Validation Workgroup

25. Coronary artery bypass surgery (CABG)?

        YES__ (attach copy of procedure note)   NO__   UNKNOWN__

        a.   Date: __ __/__ __/__ __ __ __

26. Defibrillation?

        YES__   NO__   UNKNOWN__

        a. Date: __ __/__ __/__ __ __ __

27. CPR/ACLS?

        YES__   NO__   UNKNOWN__

        a.   Date: __ __/__ __/__ __ __ __

Section 7: Stress Test

28. Was there an abnormal result from a stress test (ETT, exercise echocardiography, exercise/pharmacologic nuclear study, dobutamine echocardiography)?

        YES (attach copy of report) __

        NO, test was normal __

        NO, test not done or results not available __

AMI Validation Workgroup

Section 8: Disposition

29. Discharge status

   ALIVE ___ (go to item 30)

   DEAD (include cause of death if noted)_____

   29a. Patient dead on arrival__

   29b. Patient died in the emergency room__

   29c. Other/Unknown__

   UNKNOWN __

30. Was patient transferred <u>to</u> another hospital?

   YES__   NO__   UNKNOWN__

Section 9: Post-mortem

31. Autopsy performed?

   YES (attach copy of report)__   NO__   UNKNOWN___

Section 10: Materials available for review

32. Was a copy of the discharge summary available?   YES__   NO__

33. Was a copy of the history and physical available?   YES__   NO__

34. If patient was transferred <u>from</u> another hospital,
      was a copy of the transfer records available?   YES__   NO__   N/A__

35. Were copies of cardiac biomarker results available?   YES__   NO__

36. Were copies of ECGs available?   YES__   NO__

37. Was a copy of the autopsy report available?   YES__   NO__   N/A__

AMI Validation Workgroup

N. APPENDIX N. ABSTRACTION MANUAL

Mini-Sentinel: AMI Validation

Instructions for Completing

Myocardial Infarction Abstraction Form

The purpose of this abstraction form is to collect and code data from components of the medical record to use in validation of discharge diagnosis codes for acute myocardial infarction (MI).

The MI may be the reason for the hospitalization or it may be a new event that occurs while the patient is hospitalized for an unrelated diagnosis.   The hospital chart will be the only source used to abstract data.

Unless otherwise instructed questions will be coded based upon documentation by an MD-DO-NP-EMT; exclude medical student's notes unless countersigned by a physician.

Many questions will be answered with a 'yes, no, unknown, or unavailable'. Certain questions, when answered 'NO', will have a built in "skip pattern" meaning that any follow-up question(s) related to that specific question will be passed over and the program will take you to the next appropriate question to be answered.

Missing dates and time will be coded using a 9. Example: 99/99/9999 or 01/99/2010 or 99:99.
Missing quantitative data will be coded according to the instructions for each specific question.

If a clear 'yes or no' is not stated, use the following synonyms to code the question:

NO		YES	
Rule out (or "R/O")		Likely	Mild
Suggestive	May be	Apparent	
Equivocal	May represent	Consistent with (or "C/W")	
Suspicious		Probable	
Questionable		Definite	
Possible		Compatible with	
Uncertain		Highly suspicious	
Reportedly		Presumably	
Could be		Borderline	
Perhaps		Representing	
Low probability		Minimal	
Might be		Thought to be	

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For each extracted medical record, the Data Partner will provide a unique 'Case ID' that will appear on all copied materials. This number should be entered on screen 1 of the access database and will appear in the upper portion of each subsequent screen of the database. Please check that this screen number matches the number on the extracted medical record materials as you move through each subsequent screen.

Administrative Information

Case ID:
    An internally generated ID code that will allow the Data Partner to link back to original records but will not be identifiable beyond the Data Partner. *Please record this number on the first screen of the access database.*

Abstractor's Initials:
    Enter your initials in space provided.

Abstraction Date:
    Enter the date you are completing this abstraction in space provided.

Data Partner Name:
    Select name of the Data Partner from the dropdown menu provided.

Section 1: General information

1. Date of admission:
    This item relates to the date the patient was admitted to the hospital. If the patient was transferred from another hospital or an emergency room, the date of admission will still be that date on which the patient was admitted to the hospital.

2. Date of discharge:
    This is the date the patient was discharged from the hospital. Discharge is defined as leaving to go to: home, skilled nursing facility, rehabilitation, other acute care hospital, AMA ("against medical advice"), hospice or death.

3. Was this patient transferred **from** another hospital?:
    Code 'YES' if the patient had been admitted to another hospital or was seen in an outside emergency room prior to their transfer to the hospital. Code 'NO' if there is no evidence in the chart indicating that the patient was admitted to another hospital or seen in an outside emergency room.

4. Race/Ethnicity:
    If information on patient's race or ethnicity is available, check all that apply. If patient's race is not available, mark 'UNAVAILABLE/UNKNOWN'. If race or ethnicity is known but is different from options on screen, mark 'OTHER'.

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5. Age:
   Indicate patient's age in years. If not able to be found, check box marked 'UNAVAILABLE'.

6. Gender:
   Indicate whether patient is male or female. If not able to be found, check box marked 'UNAVAILABLE'.

Section 2: Medical history

7. Was there a documented acute episode of symptoms consistent with cardiac ischemia? (Symptoms include: chest pain/pressure/tightness/burning, left arm pain, jaw or neck pain, shortness of breath (SOB)/dyspnea, sweating/diaphoresis, nausea, vomiting):
   Code 'YES' if there is documentation of one or more of above-listed symptoms. Code 'NO' if no symptoms or if none of the symptoms listed above. If there is no description available of the patient's symptoms, code 'UNKNOWN'. If the patient is nonverbal at presentation and the records document that the presence or absence of symptoms cannot be determined, code 'UNKNOWN'.

8. Is there evidence in the patient records of a prior myocardial infarction?:
   Code 'YES' if there is an explicit statement by a physician/NP of a prior history of MI. If YES, question 8a will appear; please answer it. If NO, proceed directly to question 9.

   8a. If YES, was the patient discharged within the past 10 days?:
       Code 'YES' if there is an explicit statement by a physician/NP of a hospital discharge in the past 10 days. Code 'NO' if there is an explicit statement indicating patient discharged more than 10 days ago. If information unavailable, code 'UNAVAILABLE.'

Section 3: Biomarkers

Please record all pre-hospital biomarker levels by clicking on the pre-hospital tab provided (q. S1-S7). Pre-hospital lab values should include lab standards (the reference values) and units where available. All instructions are the same (see below) for pre-hospital and current hospital biomarkers.

Biomarker Laboratory Standards (q. 9-14)

For each specified biomarker, record the requested laboratory standards in the spaces provided.

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Upper reference limit: Record this as it appears in the lab printouts. If a range is given (example: <0.03; ≤0.03) please select the appropriate sign (< or ≤) from the dropdown menu. If only a number is given, enter the number as free text and do not select an option from the dropdown. If a normal value is provided as a range (for example CPK 61-224) please enter this range into the box entitled "Upper Reference Limit (URL)"

Indeterminant range: Sometimes labs provide a middle range of values called "equivocal," "indeterminant," etc. If available, enter the given range as written. If unavailable, leave blank.

Abnormal (consistent with necrosis): Record this as it appears in the lab printouts. If a range is given (example: >0.03; ≥0.03) please select the appropriate sign (>or ≥) from the dropdown menu. If only a number is given, enter the number as free text and do not select an option from the dropdown. There are multiple ways this upper value may be described including "consistent with AMI", "possible MI", "positive for myocardial injury."

Code units as follows from the dropdown menu: 1= ng/mL; 2=Units/L; 3=μg/L; other. **DO NOT FORGET TO ENTER THESE.**

99th percentile of the URL*
*If lab or chart provides a 99th percentile of the URL for Troponin I or T, please enter: This is a piece of information that is distinct from the previous lab standard cut-offs. This should ONLY be filled out if the lab or chart EXPLICITLY reports something called a "99th percentile," "99th percentile of the upper reference limit (URL)," "99th centile" or "99th centile of the upper reference limit (URL)". Enter as free text.

 If the specific biomarker was not done, leave blank.
**If you find more than one type of Troponin used in one patients' chart, please use the space available to note the first type(s) of Troponin I and T, then record the corresponding lab standards and values. Please use the spaces marked "Troponin (other):_____", specify the type as free text, then record the corresponding lab standards and values.

Biomarkers Measurements (q. 15-16.xx):
- *Initial levels* will be defined as the **first biomarkers** drawn at the hospital.
- *Subsequent levels* should include all subsequent biomarkers.
- Use date and time the blood was drawn as recorded on the lab report **(i.e. Time collected)**. If collection date and time is not recorded, then use date and time the blood sample arrived in lab or date and time blood was processed in the lab. If (and only if) no lab reports are available, record values if they appear in chart (Emergency room note, history and physical, discharge summary, transfer summary).

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- If you have no lab date, code as 99/99/9999. If you do not have information on the time, code the time as 99:99.
- If a specific test was not performed leave blank.
- Please DO NOT SKIP boxes – enter consecutive biomarkers without leaving any blanks.
- If a value is reported as a range, e.g. CPK = 20-30, record as written. If value is reported using a "<" or "≤" sign then indicate this using dropdown menu.
- Handwritten biomarkers from the chart should not be entered UNLESS THEY ARE THE ONLY AVAILABLE BIOMARKERS. If lab reports or other sources for biomarker information ARE available, please note any discrepancies between these and handwritten biomarkers IN THE NOTES SECTION.
- In the event that there are multiple pages of biomarker information with no time or date, please enter data in the order it appears in the chart.

Section 4: Electrocardiogram(s)
*Attach copies of **all** available electrocardiograms.*

17. Were any 12 lead ECGs taken during this admission?:
    Code 'YES' if ECGs are available OR if described in the chart but unavailable. If no ECGs available AND if no ECGs referred to in chart, skip to question 19.

18. First ECG taken after arrival at the surveillance hospital:
    Record date and time of first ECG. If ECG not available, code 99's for date and time. If ONLY ONE ECG is available for hospital stay but it is not clear whether this was the first taken, record date and time for this ECG here.

19. Were there other ECGs available?:
    Code 'YES' if other ECGs are available.

20. Last ECG on this admission:
    Record date and time of last ECG. If ECG not available, code 99's for date and time.

Section 5: Echocardiogram(s)
*Attach copies of **all** available echocardiogram reports.*

21. Was an echocardiogram performed during this admission?:
    Code 'YES' if echocardiogram report is available OR if echocardiogram is described or referenced in chart. Code 'NO' if echocardiogram report is not available and if no echocardiogram is described or referenced in chart. Code 'UNKNOWN' if it is unclear from the chart whether one was done. (Example: if the initial history and physical states that an echo will be performed but there are no subsequent descriptions or references to it and no report).

22. Is an echocardiogram report or interpretation available?:
    Code 'YES' if report available.

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Section 6: Procedures or Interventions Performed During Hospitalization
If these were performed outside of the hospital prior to admission (as in the case of EMT-initiated CPR), or if they were performed at an outside hospital prior to transfer to the hospital, please describe them in the notes section. But only answer 'YES' if the procedure or intervention was administered DURING THE HOSPITAL STAY.

23. <u>Was a thrombolytic agent administered?</u>:
       Code 'YES' if a medication called a "thrombolytic" or "fibrinolytic" was given to dissolve clots during heart attack. Thrombolytics: reteplase (r-PA or Retavase), alteplase (t-PA or Activase), urokinase (Abbokinase), prourokinase, APSAC, streptokinase, Streptase, Eminase (Anistreplase), tenecteplase (TNKASE).

24. <u>Cardiac catheterization with or without percutaneous coronary intervention (PCI)?</u>:
       Code 'YES' if a cardiac catheterization was performed, with or without PCI, angioplasty or cardiac stent placement. If 'YES', include copy of report. Code 'UNKNOWN' if it is unclear whether any of these occurred. Record the date if available. If not available, code 99's.

25. <u>Coronary artery bypasses surgery (CABG)?</u>
       Code 'YES' if patient underwent coronary artery bypass surgery. If 'YES', include copy of operating room report. Code 'UNKNOWN' if it is unclear whether this occurred. Record the date if available. If not available, code 99's.

26. <u>Defibrillation?</u>:
       Code 'YES' if patient required defibrillation. Code 'YES' only if the word "defibrillation" or "defibrillated" appears in the chart OR if the chart indicates that a patient was "shocked" <u>due to</u> "Vtach/ventricular tachycardia/Vfib/ventricular fibrillation." Code 'UNKNOWN' if it is not clear whether patient was defibrillated. Record the date if available. If not available, code 99's.

27. <u>CPR/ACLS?</u>:
       Code 'YES' if there is documentation that the patient underwent CPR or ACLS (advanced cardiac life support). Record the date if available. If not available, code 99's.

Section 7: Stress Test
*Attach copies of **all** available stress test reports.*

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28. <u>Was there an abnormal result from a stress test (ETT, exercise echocardiography, exercise/pharmacologic nuclear study, dobutamine echocardiography)?</u>
Code 'YES' and attached copy of the report if test result is described as consistent with ischemia (including possible or probable ischemia) or as abnormal in any other way. Code 'NO' if report is described as normal or negative for ischemia. If the interpretation is unclear, code 'YES' and include copy of report. If test not done or results not available, code 'NO, test not done or results not available'.

Section 8: Disposition

29. <u>Discharge status:</u>
Code 'ALIVE' if patient discharged alive, then skip to question 28. If documented death in hospital, code 'DEAD' and note cause of death in free text section if available. Code 'UNKNOWN' if it is unclear whether the patient was discharged alive or whether patient died. (Coding 'UNKNOWN' should be extremely rare. Please review chart to make sure you cannot determine alive vs. dead at discharge).

If you code 'DEAD' you will see question 29a. For 29a, check box if patient was dead on arrival, otherwise leave blank.   For 29b, check box if documented death in emergency room (or in the emergency room waiting area), otherwise leave blank. For 29c check box labeled 'Other/Unknown' if patient died elsewhere or if timing/location of death is not available.

If you code 'ALIVE' you will not be asked whether an autopsy was performed. If you code 'DEAD' or 'UNKNOWN' you will be asked question 31 in Section 9.

30. <u>Was patient transferred **to** another hospital?:</u>
Code 'YES' if documentation of transfer to another hospital, for instance, as mentioned in discharge summary or transfer summary. Code 'UNKNOWN' if unclear whether patient transferred to another hospital at discharge.

Section 9: Post-mortem
You will only be asked this if you code 'DEAD' for Section 8, indicating that the patient died in the hospital, or if you code 'UNKNOWN' for Section 8, indicating you are not sure whether patient died in the hospital.

31. <u>Autopsy performed?:</u>

IF patent died:
Code 'YES' if patient died and autopsy was performed. If 'YES' is coded, include copy of report. Code 'NO' if patient died but no autopsy was performed. Code 'UNKNOWN' *only* if patient died *and* it is unclear from the chart whether an autopsy was performed.

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Section 10: Materials available for review
Be sure Case ID number in the upper right hand corner of all materials.

32. <u>Was a copy of the discharge summary available?</u>:
    Code 'YES' if copy available.
33. <u>Was a copy of the history and physical available?</u>:
    Code 'YES' if copy available.
34. <u>If patient was transferred from another hospital, was a copy of the transfer records available?</u>:
    Code 'YES' if copy available. Code 'N/A' if patient was not transferred from another hospital.
35. <u>Were copies of cardiac biomarker results available?</u>:
    Code 'YES' if copies available.
36. <u>Were copies of ECGs available?</u>:
    Code 'YES' if copies available.
37. <u>Was a copy of the autopsy report available?</u>:
    Code 'YES' if copy available.

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O. APPENDIX O. ADJUDICATION FORM

MINI-SENTINEL: AMI VALIDATION
2010-2011 ADJUDICATION FORM

CASE ID: _____   DATE OF REVIEW: ☐☐ / ☐☐ / ☐☐☐☐

CRITERIA FOR DEFINITE ACUTE MYOCARDIAL INFARCTION (MI)[*]
CHECK IF PRESENT:

☐ DETECTION OF RISE AND/OR FALL OF CARDIAC BIOMARKERS (PREFERABLY TROPONIN) ABOVE THE 99TH PERCENTILE OF THE UPPER REFERENCE LIMIT (URL)[**] ACCOMPANIED BY AT LEAST ONE OF THE FOLLOWING:

    ☐ ISCHEMIC SYMPTOMS

    ☐ ECG CHANGES INDICATIVE OF NEW ISCHEMIA (NEW ST-T CHANGES OR NEW LBBB)

    ☐ DEVELOPMENT OF PATHOLOGICAL Q WAVES IN ECG

    ☐ IMAGING EVIDENCE OF NEW LOSS OF VIABLE MYOCARDIUM OR NEW REGIONAL WALL MOTION ABNORMALITY

☐ SUDDEN UNEXPECTED CARDIAC DEATH, INCLUDING CARDIAC ARREST, WITH SYMPTOMS SUGGESTIVE OF MYOCARDIAL ISCHEMIA, ACCOMPANIED BY AT LEAST ONE OF THE FOLLOWING:

    ☐ NEW ST ELEVATION

    ☐ NEW LBBB

    ☐ DEFINITE NEW THROMBUS BY CORONARY ANGIOGRAPHY OR AUTOPSY (BUT DYING BEFORE BLOOD SAMPLES COULD BE OBTAINED OR BEFORE APPEARANCE OF CARDIAC BIOMARKERS IN BLOOD)

☐ PCI RELATED MI: ELEVATIONS IN CARDIAC BIOMARKERS GREATER THAN 3 X 99TH PERCENTILE URL DURING THE FIRST 48 HOURS POST-PCI (IN SETTING OF NORMAL BASELINE TROPONIN VALUES).

☐ CABG RELATED MI: ELEVATIONS IN CARDIAC BIOMARKERS GREATER THAN 5 X 99TH PERCENTILE URL DURING THE FIRST 72 HOURS POST-CABG (IN SETTING OF NORMAL BASELINE TROPONIN VALUES) AND ONE OF THE FOLLOWING:

    ☐ NEW PATHOLOGICAL Q WAVES

    ☐ NEW LBBB

    ☐ ANGIOGRAPHICALLY DOCUMENTED NEW GRAFT OR NATIVE CORONARY ARTERY OCCLUSION

    ☐ IMAGING EVIDENCE OF NEW LOSS OF VIABLE MYOCARDIUM

☐ PATHOLOGICAL FINDINGS POSTMORTEM OF AN ACUTE MI

[*]MI = MYOCARDIAL INFARCTION
[**]URL = UPPER REFERENCE LIMIT
○ **NOTE:** IF THE 99th PERCENTILE OF THE UPPER REFERENCE LIMIT (URL) FROM THE RESPECTIVE LABORATORY PERFORMING THE ASSAY IS NOT AVAILABLE, THEN THE URL FOR MYOCARDIAL NECROSIS FROM THE LABORATORY SHOULD BE USED. IF THE 99th PERCENTILE OF THE URL OR THE URL FOR MYOCARDIAL NECROSIS IS NOT AVAILABLE, THE MI DECISION LIMIT FOR THE PARTICULAR LABORATORY SHOULD BE USED AS THE URL.

TYPE OF EVENT

DEFINITE MI_____

PROBABLE MI_____

    EXPLAIN WHY NOT 'DEFINITE': _____

    _____

NO MI_____

UNABLE TO DETERMINE____

    WHAT DATA WERE NEEDED BUT NOT AVAILABLE?

    ☐ CARDIAC BIOMARKERS

    ☐ ECGs

    ☐ INFORMATION ON ISCHEMIC SYMPTOMS

    ☐ OTHER:_____

ECG manifestations of acute myocardial ischaemia (in absence of LVH and LBBB)

ST elevation

New ST elevation at the J-point in two contiguous leads with the cut-off points: ≥0.2 mV in men or ≥0.15 mV in women in leads V_2 –V_3 and/or ≥0.1 mV in other leads

ST depression and T-wave changes

New horizontal or down-sloping ST depression ≥0.05 mV in two contiguous leads; and/or T inversion ≥ 0.1 mV in two contiguous leads with prominent R-wave or R/S ratio ☺1

ECG changes associated with prior myocardial infarction

Any Q-wave in leads V_2 –V_3 ≥0.02 s or QS complex in leads V_2 and V_3

Q-wave ≥0.03 s and ≥0.1 mV deep or QS complex in leads I, II, aVL, aVF, or V_4 –V_6 in any two leads of a contiguous lead grouping (I, aVL,V_6;V_4 –V_6; II, III, and aVF)[a]

R-wave ≥0.04 s in V1 –V2 and R/S ≥1 with a concordant positive T-wave in the absence of a conduction defect

[a]The same criteria are used for supplemental leads V_7 – V_9, and for the Cabrera frontal plane lead grouping.

P. APPENDIX P. INFORMATION ON CHARTS RECEIVED

	DP1	DP2 Site A	DP2 Site B	DP2 Combined	DP3	DP4 Site A	DP4 Site B	DP4 Site C	DP4 Combined	Total
Number Requested	38	19	19	38	38	13	13	13	39	153
Number Obtained	32, 84.2%	19, 100.0%	19, 100.0%	38, 100.0%	35, 92.1%	12, 92.3%	13, 100.0%	13, 100.0%	38, 97.4%	143, 93.5%
Number UnObtained	6, 15.8%	0, 0.0%	0, 0.0%	0, 0.0%	3, 7.9%	1, 7.7%	0, 0.0%	0, 0.0%	1, 2.6%	10, 6.5%
Avg Size of Chart (in pages)	329.72	35.16	54.89	45.02	210.37	97.58	45.31	107.62	83.50	125.6
Charts from Own Hospital	32, 100.0%	0, 0.0%	, 0.0%	0, 0.0%	0, 0.0%	12, 100.0%	0, 0.0%	13, 100.0%	25, 65.8%	57, 39.9%
Avg No of Components	7.31	7.79	8.50	8.14	7.68	6.92	8.54	7.69	7.72	7.8
Total No of Components	234, 52.2%	148, 55.6%	159, 59.8%	307, 57.7%	261, 53.3%	83, 49.4%	111, 61.0%	100, 54.9%	294, 55.3%	1096, 54.7%
Admin Hist/Physical	31, 96.9%	19, 100.0%	15, 78.9%	34, 89.5%	35, 100.0%	9, 75.0%	13, 100.0%	13, 100.0%	35, 92.1%	135, 94.4%
Discharge Summary	28, 87.5%	19, 100.0%	18, 94.7%	37, 97.4%	30, 85.7%	10, 83.3%	13, 100.0%	13, 100.0%	36, 94.7%	131, 91.6%
Transfer Records	6, 18.8%	2, 10.5%	11, 57.9%	13, 34.2%	9, 25.7%	2, 16.7%	6, 46.2%	10, 76.9%	18, 47.4%	46, 32.2%
Cardio Consult Notes	21, 65.6%	9, 47.4%	18, 94.7%	27, 71.1%	28, 80.0%	8, 66.7%	11, 84.6%	9, 69.2%	28, 73.7%	104, 72.7%
Autopsy Reports	2, 6.3%	3, 15.8%	0, 0.0%	3, 7.9%	1, 2.9%	1, 8.3%	2, 15.4%	0, 0.0%	3, 7.9%	9, 6.3%
EMT/Ambulance Notes	6, 18.8%	11, 57.9%	2, 10.5%	13, 34.2%	5, 14.3%	1, 8.3%	2, 15.4%	6, 46.2%	9, 23.7%	33, 23.1%
Emergency Dept Notes	24, 75.0%	18, 94.7%	14, 73.7%	32, 84.2%	26, 74.3%	7, 58.3%	12, 92.3%	11, 84.6%	30, 78.9%	112, 78.3%
12 lead EKG Copies	30, 93.8%	17, 89.5%	19, 100.0%	36, 94.7%	30, 85.7%	11, 91.7%	13, 100.0%	13, 100.0%	37, 97.4%	133, 93.0%
Lab Reports	32, 100.0%	17, 89.5%	19, 100.0%	36, 94.7%	33, 94.3%	9, 75.0%	13, 100.0%	13, 100.0%	35, 92.1%	136, 95.1%
Cardiac Catherization Report	16, 50.0%	12, 63.2%	15, 78.9%	27, 71.1%	25, 71.4%	9, 75.0%	12, 92.3%	5, 38.5%	26, 68.4%	94, 65.7%
PCI Report	11, 34.4%	7, 36.8%	11, 57.9%	18, 47.4%	16, 45.7%	7, 58.3%	5, 38.5%	2, 15.4%	14, 36.8%	59, 41.3%
Bypass Surgery Report	4, 12.5%	3, 15.8%	3, 15.8%	6, 15.8%	3, 8.6%	2, 16.7%	0, 0.0%	1, 7.7%	3, 7.9%	16, 11.2%
Stress Tests Report	4, 12.5%	1, 5.3%	2, 10.5%	3, 7.9%	2, 5.7%	0, 0.0%	0, 0.0%	0, 0.0%	0, 0.0%	9, 6.3%
Echocardiogram reports	17, 53.1%	10, 52.6%	12, 63.2%	22, 57.9%	23, 65.7%	8, 66.7%	9, 69.2%	4, 30.8%	21, 55.3%	83, 58.0%

Q. APPENDIX Q. TIMELINE FOR COMPLETION OF THE MINI-SENTINEL ACUTE MYOCARDIAL INFARCTION (AMI) VALIDATION TASKS

Task	Completed date*	Estimated Time to Complete
Develop AMI definition and algorithm	Month 1.5	6 weeks
Finalize a sampling strategy to identify likely AMI cases	Month 2	2 weeks
Develop list of data elements needed from each chart	Month 2	8 weeks
Establish contacts and process at each Data Partner for chart request	Month 2	4 weeks
Develop, test, and finalize SAS program to distribute to Data Partners to identify and sample likely AMI cases	Month 2.5	2 weeks for MSOC development, testing and distribution 2 weeks for Data Partners to run program and return results
Develop, test, revise and finalize abstraction process	Months 4-5	Process completed for start of abstraction: 11 weeks Revised process and database to facilitate data collection: 16 weeks
Develop, test, revise and finalize adjudication process	Months 4-5	16 weeks
Request, obtain, and redact charts for actual AMI validation and forward all electronic copies of redacted charts to Operations Center	Month 7	16 weeks
Abstraction	Month 7.5	12 weeks
Adjudication	Month 8	10 weeks
Calculate positive predictive value	Month 8	1-2 weeks
Complete draft report and submit for review	Month 8.5	Written and updated throughout project. Approximately 4 weeks time in total.
Write and submit final report to FDA based on feedback from MSOC, Protocol Core, and FDA	Month 9	2-3 weeks

*All dates measured from start of project (Month 0)