VALUE CASE FOR THE USE OF ELECTRONIC HEALTH RECORDS IN CLINICAL RESEARCH: PROCESSES TO SUPPORT CORE RESEARCH DATA ELEMENT EXCHANGE

EHR Clinical Research Value Case Workgroup

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1. Background

The vast majority of clinical research study protocols require the collection of core research data elements[1] that provide specific detailed information about key aspects of the medical care and health information of individual research participants. Clinical research requires the collection of information about research participants from their medical history and healthcare experiences. For clinical trials, longitudinal studies, outcomes research, and public health reporting, an Electronic Health Record (EHR) is increasingly being used to record and document this information[1]. Ohmann and Kuchinke state that "Clinical research has for a long time lagged behind in the implementation of an adequate information technology (IT) infrastructure to enable networked collaborative research[2]."

It has been deemed valuable by the work group and the larger health care community that enabling the use of information from health care settings would improve the efficiency and effectiveness of clinical research processes[3]. The broad topic of clinical research encompasses many domains of data and their transactions. The Biomedical Research Integrated Domain Group (BRIDG) Model is an effort to map the processes of clinical research to define areas where standards exist and where they need to be developed[4]. A high-level survey of the landscape of standards and interoperability specifications was conducted by the work group. Subsequently, the work group established a vision document[2] describing the gap between current and desired future states for the use of EHR in clinical research. Thereafter, the group used a prioritization process to map out incremental steps to accomplish the goal of EHR information use for clinical research. The highest priority was given to the ability to transact a core set of research data elements from the EHR into clinical research systems. This Value Case comprises the first contribution and provides a foundation for future Value Cases to define processes for EHR support of clinical research globally.

2. Introduction

This document contains two key sections; a description of the data elements, transactions and workflow required to support use of EHR data in clinical research; and a value proposition for the overall area of clinical research. This Value Case addresses the availability of common information in the EHR for clinical studies undertaken for many purposes, including academic medical research and clinical trials for regulatory submission. One major challenge is that this information is often collected in disparate ways without the advantage of common ontologies that allow semantic and syntactic interoperability. The Value Case also addresses key processes for transacting data that support reporting of information to the institutional review board, clinical trial registries, clinical research sponsor or other partners; support of data verification; electronic (digital) signatures; audit trails and other regulations relevant to electronic record

[1] Core research data elements are key clinical information commonly recorded during the course of standard care.

[2] http://publicaa.ansi.org/sites/apdl/EHR%20Clinical%20Research/Forms/AllItems.aspx

retention (security); subject privacy and confidentiality; and permissions for data access. Due to variability in adoption rates among health care settings and the design heterogeneity of EHR systems, this Value Case necessarily focuses on the utility of gleaning a core set of data elements from information contained in an EHR and the related workflow for clinical research purposes, independent of the platform or system in use.

2.1. Value Case Description

This Value Case conveys three requirements for the ability of an EHR to support basic information needs for most if not all clinical research activities. First, it will describe the processes necessary to move data from one system to another to enable EHR data to be used in the clinical research endeavor and improve related workflow for an investigator to contribute to research along with clinical care. These processes include the support of data verification, audit trails and other regulations relevant to security, subject privacy and confidentiality, and permissions for data access. Second, this Value Case will articulate the data elements commonly present in an EHR that are critical to a broad range of clinical research activities. Finally, it will articulate the value proposition for the use of harmonized standards and interoperability specification for the use of EHR data to support clinical research studies.

2.2. Value Case Scope

This Value Case was developed to support the stakeholders engaged in various types of clinical research, including, but not limited to, regulated clinical trials, prospective randomized controlled trials, interventional trials, observational and epidemiological studies. Using an incremental approach to closing the described gaps, this Value Case covers the exchange of core dataset information already present in an EHR into a clinical research systems of varying degrees of sophistication and the related workflow associated with such a transactions. There are many additional clinical research management applications that can benefit from the ability to effectively communicate among information sources (e.g. clinical trials recruitment, adverse event reporting, regulatory compliance, financial information reconciliation, etc.) that will need to be addressed in additional Value Cases. Major benefits of the ability to access EHR core dataset information for clinical research are to ensure the safety of research participants, improve data quality by reduction of transcription and re-entry of data, and decrease the burden of research for clinicians.

To achieve the goal of standards-based accessibility of a core research dataset from the EHR for use in clinical research, this Value Case will address the following: processes for transacting data, data elements and terminology, the perspectives of actors within the clinical research process, scenarios and workflow integration during the accessing of information, value accrued in general and to specific stakeholders through accessibility of information, and data security and retention issues.

3. Integral Processes and Data Elements for the Transaction of Core Research Data from EHR to Support Clinical Research

Here we describe the exchanges of information that occur between a transactional EHR system used for health care and clinical research. Additionally, details about and context for the core data elements in the EHR important to support clinical research activities are described.

3.1. *Processes for Transacting Data*

The following diagram depicts the flow of information from the EHR in transactional clinical systems, to an enterprise clinical repository to which researchers have access, and finally to a sponsor, regulator or other final repository of core research data elements. Each of the exchanges depicted below (A-D) transact modified subsets of the same information, but have specific processes associated that filter appropriate data, control access, and other administrative functions. The processes necessarily address issues of de-identification, privacy and security. Supplemental information may need to be collected or added to obtain the final research repository.

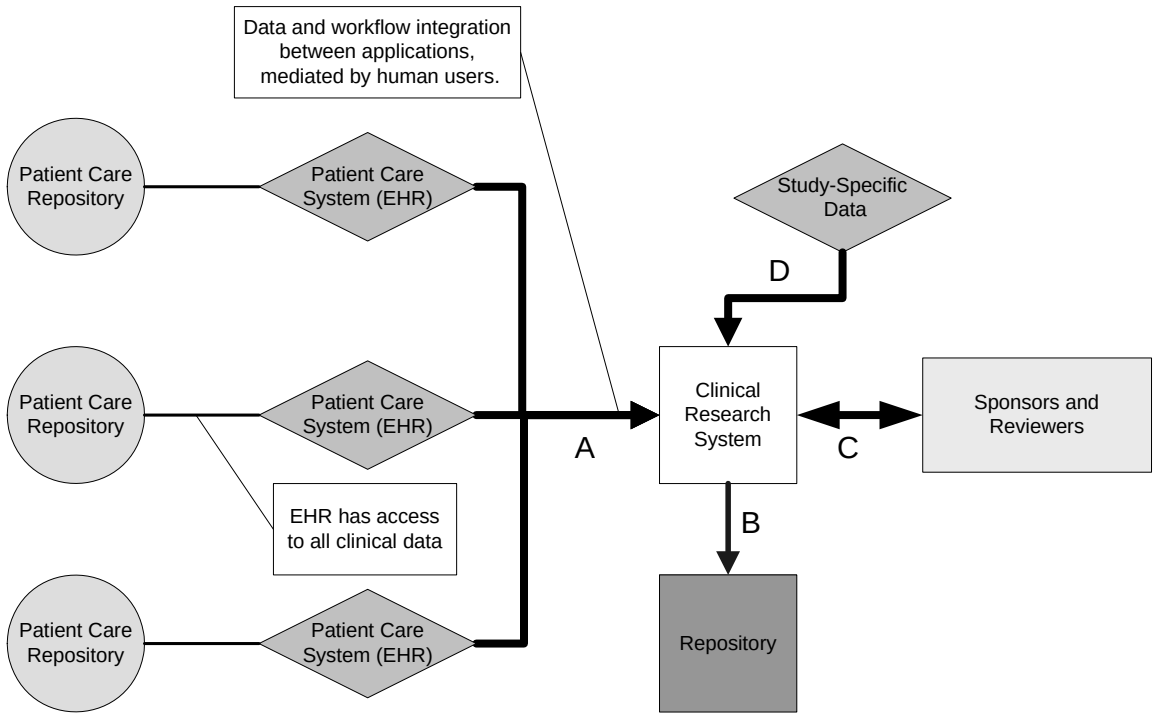

Figure 1. Systems and Perspectives in Core Research Data Elements Exchange
A) Data exchange between clinical EHR and organizational clinical research repository or data warehouse.
B) Data exchange between organizational clinical research repository and study-specific database.
C) Reporting of data to sponsor, regulatory or other agency.
D) Entry of data not present in the EHR that represent study-specific information.

3.2. *Data Elements and Terminology*

Below are described a set of data elements commonly present in the EHR that are used in a broad range of clinical research and public health reporting activities. Where possible, controlled terminology should be specified.

- Planning and Reporting Requirements
  - Informed consents
  - Eligibility Verification
  - Study design
- Subject Demographics
  - Subject identifier
  - Date of birth
  - Sex
  - Ethnic/cultural background
  - Native language
  - Date and time collected
- Prior and Concomitant Medications
  - Medication
  - Indication
  - Dose
  - Timing of medication
  - Route
  - Rate
  - Length of time on medication
  - Date and time collected
- Medical History
  - Type of history
  - Allergies
  - Surgeries
  - Family history
  - Diet
  - Exercise
  - Concomitant therapies
  - Date and time collected
- Physical Examination
  - Body system examined
  - Results
  - Clinical significance
  - Date and time collected
- Substance Use (e.g. Habits)
  - Type of substance
  - Occurrence of use
  - Frequency and duration
  - Date and time collected
- Vital Signs
  - Results and units
  - Clinical significance
  - Date and time collected
- Diagnostic Data
  - Test name
  - Test result and units
  - Clinical comments
  - Date and time collected
- Adverse Clinical Events
  - Type of event
  - Severity
  - Action taken
  - Outcome
  - Date and time collected

4. Value Case Perspectives

The perspectives listed below are entities that play a role in clinical research. This list does not correspond directly with the stakeholder list described in Section 7, which reflects the fact that value accrued does not necessarily correspond to actions taken or the entities that engage in them.

- Patients and Advocacy Organizations
- Non-Academic Clinical Practices
- Academic Research Institutions
- Clinical Research Organizations
- Regulated Research Sponsoring Organizations
- Federal Regulatory Agencies
- Health Information Technology and Clinical Research System Vendors
- Investigative Sites

- Patients and Patient Advocacy Organizations

Patients are the pool of potential subjects for clinical studies. It is important that they can access the clinical research process in the appropriate language and level of health literacy that allows their purposeful participation. Their interests are represented by patient advocacy organizations that provide support, advocacy and promote privacy protections through a variety of activities, including the funding and facilitation of clinical research. Disease registries are one way that information about different conditions is tracked. Advocacy organizations also assist in connecting patients with support and services specific to their diagnosis.

- Non-Academic Clinical Practices

Non-academic clinical practices consist of physician's practices, urgent and ambulatory care clinics, long-term care facilities and institutional health care facilities. The vast majority of health care takes place in these settings, however a disproportionately low amount of clinical research is done here. The exchange capabilities present in an EHR system could bridge the gap and allow capture of this data and facilitate the participation of these stakeholders in clinical research[5].

- Academic Research Institutions

The academic research institution perspective encompasses the investigator, research staff, clinic and institutional oversight processes involved with clinical research. Standards-based exchange of health information from an EHR facilitates clinical research in this setting during all phases of the project: experimental design, institutional review and oversight, enrollment, data collection, analysis, interpretation, publication and dissemination. Within a single institution, often multiple EHR and clinical data systems are in use and prevent the aggregation of data across the institution to suit multiple purposes. Such academic sites are now being encouraged to share data across institutions and with other appropriate groups, hence the need for a common set of standards.

- Clinical (Contract) Research Organizations

The Clinical Research Organization (CRO) may play a role in all or a subset of the activities performed by a clinical study sponsor. The CRO is responsible for the activities contracted to them by the study Sponsor and also for transferring the data, results and any other requested deliverables to the Sponsor during and/or after the completion of the research project.

- Sponsoring Organizations

Sponsoring organizations or study sponsors are any organization responsible for a clinical study, including Academic Research Organizations, Federal and State public health agencies and organizations assessing quality of health care under state and national guidelines (i.e. National Committee for Quality Assurance). There are also individual investigator-sponsored studies. The term Sponsor also commonly refers to pharmaceutical, biotechnology and device companies conducting regulated clinical research. Sponsors are responsible for trial design, protocol development, data collection form development, data acquisition and management, analysis and reporting and related QA/QC. The Sponsor may chose to contract out any or all of these activities to a CRO, while still retaining full accountability for the delegated tasks. Sponsors, as well as regulators, must be able to trace the data in the final reports back to the source; if any changes are made, these must be documented (who, what, when, why) through an appropriate audit trail.

- Federal Regulatory Agencies

In the United States, the regulatory agency for food and drugs, devices and other therapies is the Food and Drug Administration (FDA). The FDA approves such products for marketing in the U.S. even if much of the research is done elsewhere. The FDA requires that data be included in the regulatory submissions for new products and are requesting data in a standard format to facilitate review and allow creation of a cross-study database. Other regulatory bodies may have additional regulations or guidelines that apply to studies done in their countries. The FDA interacts with sponsoring organizations for Investigational New Drug Applications and other regulatory submissions to approve products for the market and assure public safety. Regulatory reviewers analyze data provided by the sponsor to make decisions about approval of new therapies. If the data are in a standard format, they can apply useful tools for their reviews. Part of the review process involves auditing data submitted with applications, which requires the ability to trace data from investigator to submission, including changes made.

- Health Information Technology Vendors and Clinical Research System Vendors

Health Information Technology (HIT) Vendors develop and market EHR systems to health care systems, from individual physicians to large academic medical centers. These vendors have to incorporate the appropriate standards or mappings to standards into their products to achieve the exchange of data described in this Value Case. Clinical Research Systems Vendors may be involved in the receipt of the core dataset from an EHR system.

- Investigative Sites

Any site doing clinical research is responsible and accountable for data[3], even when it is exchanged from site to CRO and/or sponsor to regulatory agency, institutional review board (IRB) or other reporting point. For regulated studies, sites are required to follow appropriate data retention guidelines and regulations. They should also be queried and approve any changes made in the data between their site and the reporting site and may be audited to ensure the integrity of the final data included in a report, publication or submission.

5. Value Case Scenarios for the Core Research Data Elements

Underpinning the efforts to harmonize standards for data exchange and detail interoperability specifications, it is necessary to describe common situations where data transactions from an EHR system would occur to support clinical research. The value proposition is a rationale for stakeholder organization use of the harmonized standards. Below are two broad scenarios where EHR information is available for use in clinical research.

The information flow described in each of the scenarios is not fundamentally different. The processes, however, consent, access and ultimate purpose of the exchange differs between the two.

Scenario 1: Data extraction from EHR to sponsor for submission to regulatory, public health and other agencies.

This scenario describes the information flow upon enrollment of a subject into a clinical study. The steps described below apply to most types of clinical research, including clinical trials that end in regulatory submission, academic research or observational studies and studies that examine standard of care. This describes the exchange of information from an EHR to a research Clinical Data Management System (CDMS) or enterprise clinical repository (see Figure) and the associated workflow.

Enrollment. Notification of the CRO or Sponsor should occur when a subject is enrolled in the study (i.e. deemed eligible per the research protocol). The subject should receive a study number linking the subject to the source medical record, but providing a de-identification mechanism such that the CRO or sponsor does not receive any information that could identify the subject (e.g., subject's name, social security number, address or any other identification information).

Data Collection. A case report form for a clinical protocol is pre-populated with data identified within the EHR. Core research data elements can be identified using triggers, case report form designs or trial designs from protocols. Following confirmation by the investigator or study coordinator that these data are correct and accurate, they can be exported from the EHR into the CDMS (housed by a research system vendor, CRO or

[3] Pursuant to 21CFR312.62 Investigator record-keeping and record retention

study sponsor) or other clinical research system. The transfer could occur at regular intervals or done in real-time in regions with advanced health information exchanges. The eSource data are maintained in the EHR at the investigative site or in an appropriate archive format at the site or at a third party; this source data includes the audit trail. Core dataset information present in the EHR would be available to the CDMS. Additional data, specific to the clinical study, may be collected and sent to the CDMS in addition to populating the EHR as appropriate[4] (to retain the eSource record). It would also be possible to use existing EHR systems to capture study-specific data in a systematic fashion. Thus, the information flow must be bidirectional for various purposes in the research process, such as Source Data Verification. This would streamline the workflow for the investigative site. Ideally, the associated terminology would be harmonized between EHR and research systems.

Source Data Verification. Data verification may take place initially at the site during the study and at the completion of the clinical trial. Queries about anomalous data can be sent by the sponsor or CRO (via the CDMS) to the EHR system for verification.

Institutional Review and Data Safety Management Boards. Information may need to be exchanged between the clinical study and Data Safety Management Boards (DSMB), Institutional Review Boards, ethics committees, regulators or government funding agencies to ensure the safety of subjects in the study, as specified in the research protocol. Real-time access to the data also allows monitoring of event rate, compliance and adherence to study protocol, which may trigger the DSMB to conduct a safety review of the study before the protocol-specified DSMB assessment.

Data Re-use. Data collected in standard format from the EHR allows the information to be warehoused for future analyses. Rigorous data definitions facilitate pooling data from multiple studies. When a clinical research study is being planned, information is sent to a trial registry (see Scenario 2). At the conclusion of the trial, results should be published in a trial registry (e.g. clinicaltrials.gov) or peer-reviewed journal.

Submission of Data to Regulatory Agency. Submission of data to a regulatory agency is primarily done with data from a combined set of clinical trials for a given therapy. A warehouse is also useful for this purpose. For each study, statisticians within the Sponsor or CRO use trial data from the CDMS to produce reports, tables, figures and listings. In addition, an integrated safety database and an integrated efficacy database are created for the submission. All of these data would already be in the standardized format in which they were captured from the EHR; additional standards are used to transport and display the integrated data and statistical analyses for the regulatory reviewers.

Scenario 2: Exchange of information from EHR to registries or other databases.

This scenario describes the exchange of health information between EHR and a patient registry or database.

Database. The database or registry may be maintained at a single institution and enable aggregation and analysis of data collected by multiple EHR systems present within the institution. The database or registry may also be maintained by a third party, such as a

[4] For example, indicators to a health care provider that a patient is in a clinical trial, but does not include incomplete research data that may compromise care.

patient advocacy organization or government agency (e.g. clinicaltrials.gov). Patients, with their physicians, submit core dataset information from the EHR directly into databases or disease registries for multiple purposes, including public health. This data transaction may include condition-specific data in addition to the core dataset information. Ideally, the submission would allow the database or registry data to be updated when changes are made in the EHR relevant to the core dataset.

Communication. The results of the trial can be conveyed back to the individual and/or their care providers once the analysis is complete. In blinded studies, the longitudinal health record should be updated to indicate to which, if any, agent or intervention the individual was exposed and any long term follow up which may be required.

Scenario 3: Exchange of information from EHR in a distributed research network

This scenario describes the exchange of information to a database within an organizational firewall. The data could be used for multiple purposes, including outcomes research, observational studies and quality measures.

Network. Data can be aggregated from a single practice with multiple providers or from multiple sites within a network. Core data from the EHR is submitted regularly into the database and pseudonymized for aggregation with other data submissions. This allows for nearly real-time tracking of data across the network.

Data Queries. Data are maintained within a security firewall of an organization. Queries can be made of the data from outside the firewall under controlled access. Users of different types can be granted different levels of access to the data.

6. Value of EHR Standards and Interoperability Specifications to Support Clinical Research

The area of EHR information use for clinical research is broad and while the standards and interoperability specifications can be articulated in an incremental fashion, the value may not accrue in a similarly incremental way. We therefore describe below the value of a fully harmonized system of EHR data support of clinical research, rather than value specifically for the core research data elements.

There are seven recurring values of Core Research Data Elements that are accrued by all stakeholders in the clinical research process:

1. The ability to engage more people in clinical research[6] thus informing healthcare with more robust information and enabling access to newer therapies for more patients
2. Reduction of errors in data[7]
3. Aggregation of data across studies
4. Data collection that is less intrusive for clinician workflow
5. Elimination of duplicate data collection (easier for researchers or investigators)
6. Real-time data reporting for safety[8]
7. Facilitated information sharing and partner communications

Each of these categories ultimately results in a clinical research process that moves new knowledge into practice in a quicker, safer, and more cost-effective manner. This means better and safer treatments for patients, better care guidance for physicians, greater return on investment for the private sector and reduced cost of effective regulation.

7. Value Case Stakeholders

Listed below are entities which garner benefit from the streamlining of clinical research processes through the ability to access information from an EHR system. While this list overlaps with the perspectives in section 4, those listed below accrue value without necessarily altering an action or interface with the clinical research endeavor.

- Patients and Advocacy Organizations
- Physicians and Caregivers
- Academic Research Institutions and Sponsors
- Clinical Research Organizations
- Institutional Oversight (e.g. Institutional Review Board, Data Safety Monitoring Boards, etc.)
- Biotechnology, Pharmaceutical and Device Manufacturers
- Federal Regulatory Agencies
- Health Information Technology and Clinical Research System Vendors
- Payers of Healthcare Services
- Government Funding Agencies
- Public Health Agencies and Health Care Quality Organizations

- Patients and Advocacy Organizations

The ability to report clinical information directly from the EHR to clinical research entities provides value for patient participants in several ways. This approach will facilitate the identification of patients interested in clinical studies[6]. It will also reduce the time requirement for participation in clinical studies by eliminating repetitive paperwork and potentially reducing additional study tests and visits by reporting data collected during the course of normal care. Well-defined and controlled mechanisms for health information exchange may help allay concerns about confidentiality via established policies, procedures and use of appropriate technology.

The use of electronic means may enable long-distance participation in clinical research for patients who might not previously had access, such as international participants and those living in rural areas[5]. Moreover, the ability to participate in clinical studies via an EHR may empower minority groups to engage with research and partake of the benefits[9].

The value of standards-based exchange of a core dataset from the EHR to advocacy organizations is ease of identifying patients, both those who are interested in the support they provide and those who are interested in participating in clinical research. This can also provide the advocacy group with access to up-to-date information about a disorder, such as rates of diagnosis.

- Physicians and Caregivers

One reason many physicians and caregivers do not participate in research is the burden of data entry and audit trails due to a historically paper-based clinical research system. The typical clinical research workflow currently requires transcription and re-entry of information into additional systems or paper case report forms. The query resolution process is even more cumbersome. Integrating the ability for clinicians to provide high quality research information without significantly impacting their workflow or ability to provide patient care would encourage more participation by this group in clinical research. Greater participation would improve the research information that informs healthcare, thereby improving patient care and providing greater opportunities for patients to access new and safer therapies.

- Academic Research Institutions and Sponsors

Standards-based exchange of data from an EHR for use in clinical research benefits the investigator and institution at all stages of the process. During protocol development and case report form design[8], the use of standardized data elements could reduce the required time by as much as 80% of the non-patient participation time[10]. Standards streamline the entire study process, including team training and communications, interactions with partners and produce higher quality data from the start of the study. The ability to screen potential study participants would reduce the study staff requirement at this stage by 20%[10]. Recruitment is also facilitated by the ability to query EHR systems to identify patients who fit specified inclusion/exclusion criteria. Data collection costs could be reduced by 80-90%[10] and the quality of data would be increased. Moreover, exchange of information between EHR and clinical study allows real-time monitoring of event rate, compliance and adherence[8]. This could allow the protocol to be amended to minimize the numbers of subjects exposed to potentially harmful outcomes and optimize the analytic capabilities of the study. EHR data capture also means that unscheduled visits and observations are captured, particularly health events that do not reach the threshold of adverse events reporting. Standardized data collection also makes possible standardized data analysis algorithms and tools and increases the power of subsequent meta-analyses. Electronic verification relieves a burden on the clinical research staff to monitor and verify data sources, freeing them for other duties involved with the trial.

- Clinical Research Organizations

The CRO accrues many of the same values described above. Additionally, the Sponsor and CRO for regulated clinical trials are responsible for audit trails for the eventual regulatory submission of clinical trial data. CROs reap additional benefits when their clients use industry standards since they can streamline and standardize their processes. This is not feasible if their Sponsors each request different formats for data collection and reporting.

- Institutional Oversight (e.g. Institutional Review Board, Data Safety Monitoring Boards, Privacy Councils, etc.)

Oversight boards evaluate protocols for human subject protection and data integrity. If the data are not sound, any conclusions drawn from the research are compromised and any risk incurred by a human subject is unacceptable. The value to this stakeholder is captured by the higher data quality and accessibility from the use of EHR data which increases the utility of the data. Furthermore, real-time monitoring of study data could indicate the need for review by a data safety monitoring board before the time scheduled in the protocol.

- Biotechnology, Pharmaceutical and Device Manufacturers

These stakeholders often operate as sponsors of clinical trials. Much of the value described above also applies to this group, as it carries the cost burden of the clinical studies. These sponsors also garner value through facilitating the process of submitting an application to Federal Regulatory Agencies[11]. Therefore, the facilitation of data collection and verification are valuable to these stakeholders. This group also accrues value with the added facilitation of safety reporting based on the transaction of data from the EHR.

- Federal Regulatory Agencies

The value to the FDA is a more comprehensive audit trail with a standardized electronic format[12]. Standardization of EHR data export to a case report form could give the FDA a better picture of the outcomes of the trial. Use of data interchange standards and controlled terminology facilitates data integration of data across trials. Regulators can review submissions in a more streamlined manner if they come in a standard format; it also enables their use of sophisticated tools.

- Health Information Technology and Clinical Research System Vendors

Developers of information systems are often faced with challenges of applying common information tools and technologies to meet vastly differently health care and research settings. For example, health information systems designed for acute care, in-patient settings may be ineffective for ambulatory care research or specialty settings. Standards harmonization activities will serve to enable broader applicability and greater customization potential across clinical care settings and research programs[11].

- Payers of Healthcare Services

Payers are increasingly looking at research opportunities to optimize the services that they provide to beneficiaries. Improvements in informatics tools to engage consumers, patients and research participants, in general, serve to support their objectives. Through greater access to information, standards harmonization and information sharing capabilities, particularly from the patient and research participant engagement in the processes through electronic means has many merits. Recent efforts by government payers to provide incentives to beneficiaries of federal health care plans to use personal health records speak to the importance of engagement that could ultimately yield greater outcomes research opportunities.

Many insurance companies collect vast amounts of data related to healthcare and perform studies using this information. However, this is currently related to coding for billing purposes and thus may not accurately reflect patient safety information, nor does it

represent high quality clinical research data[13]. A more reliable, standards-based core set of information for research purposes would augment the ability of Payers to make informed policy decisions. In addition, it would allow them to better integrate information when patients change healthcare providers and/or insurers.

- Government Funding Agencies

Government agencies often take the role of research sponsors and funders of research. For these agencies, tracking the progress of studies, with regards to recruitment and retention, and supporting accounting practices are highly valuable capabilities. In addition, studies funded by government agencies are encouraged to increase data sharing among research communities. A standards-based data exchange of a core set of information would enable such sharing and enhance the value for the public of using government funding for research.

The use of standards facilitating data exchange can overcome significant barriers in understanding and application of research. In addition, this can address the need for improved data quality in clinical research and provide new approaches to longitudinal data collection and the ability to examine interactions among research studies.

- Public Health Agencies and Health Care Quality Organizations

Public Health Agencies need to receive information about patient safety, disease outbreaks, health status of a population and health trends. The ability to populate a core set of data that would provide such information seamlessly to these agencies would be invaluable as the adoption of EHRs increases. The standardization of EHR and the facilitation of data collection in health care management systems have a critical role in assessment of quality of care. This would decrease the burden on clinicians to report such information and increase the frequency of reporting. The core set of information for research is not significantly different from the information needed for public health and quality measures.

8. Issues and Obstacles to Standards Harmonization and Interoperability Specification for EHR Information Use to Support Clinical Research

8.1. Confidentiality, Privacy, Security, and Data Access

The importance of confidentiality, privacy, and security and control of data access is critical for the participation of subjects in clinical research. Control of core dataset information resides with the subject and must be articulated during the consent process. Therefore many aspects of data access are likely to be protocol-specific. This Value Case addresses only the export of core dataset information from an EHR for clinical research purposes.

Consumer data confidentiality and privacy. Patients must be confident that the agreements made during the consent process are delivered by the electronic systems holding their personal health information.

Security and data access. Core dataset information must be accessible to clinical research staff in an accurate and up-to-date form. Access to this information, however,

may be restricted to research staff from a particular study, in the case of scenario 1, or to a more general clinical research community, as in scenario 2.

Data Access, Data Integrity and Disclosure Logs. In order to maintain an intact audit trail, sponsors and regulators will need to be able to track data from clinical studies back to source materials, in this case the EHR. Regulated trials require that data integrity be maintained through such an audit trail and record retention regulations.

8.2. Interoperability

The exchange of information across systems, sites, and settings of care is constrained today by the lack of agreed upon standards for sharing of information contained in the EHR and a cumbersome workflow process. Often there are multiple systems at a single institution that are unable to exchange information. This ultimately means that data cannot be aggregated and the full value of clinical data donated by patients is not realized.

For information to be aggregated and analyzed it must be comparable. This can only occur with data requirements or via rigorous multi-use data element standards and controlled terminology to ensure semantic interoperability. Data elements must have common identifiers, so that it is clear what type of information is being exchanged. The data must be in a standard format to allow automated processing. Units of measurements must be clearly conveyed. For non-measurement values, a standard (controlled) vocabulary must be used in conjunction with well defined metadata, and data attributes.

8.3. Regulatory Compliance

21 CFR Part 11 of the FDA's Electronic Record, Electronic Signature Regulations states several requirements for computer systems that are used in clinical research[5]. Among these are the ability to validate the system itself, an audit trail for the data exchanged, retention of records after the completion of the study, security measures, control of access to data and established policies and procedures for the use of the system during clinical research[14]. These capabilities will have to be integrated into the standards and interoperability specifications set forth to accomplish the transfer of EHR information for use in clinical research and enable confirmation of compliance of sites and sponsors.

42 CFR part 52**,** Grants for Research Projects [15] applies to all health-related research project grants administered by the Public Health Services or its components.
The Office of Management and Budget (OMB) accelerates the adoption of health information technology and utilization of EHR. OMB also develops regulations on a management of government grants. The HITECH Act of the American Recovery and Reinvestment Act imposes more stringent regulatory requirements under the security and privacy rules of the Health Insurance Portability and Accountability Act and further development of standards for electronic health records [16].

9. Information Exchange/Business Agreements

The standardization of a core dataset of clinical research information will facilitate the sharing of information between health care institutions and other organizations that have

[5] FDA Guidance for Industry Computerized Systems Used in Clinical Investigations

an interest in the data. Furthermore, this dataset will simplify contractual agreements between organizations and facilitate IRB reporting. In addition patients will need to sign appropriate informed consent documents or equivalent as required per the study/country/IRB and regulatory agency.

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