Use of Electronic Health Records in Clinical Research: Core Research Data Element Exchange

Detailed Use Case

April 23rd, 2009

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1.0 Preface

In June of 2008, the American Health Information Community (AHIC) approved a recommendation to develop a Clinical Research Use Case. The Use of Electronic Health Records in Clinical Research: Core Research Data Element Exchange Use Case document has been driven and developed by the ANSI-convened Clinical Research Value Case Workgroup to represent the AHIC prioritization process and provide context for the national agenda activities, beginning with the selection of harmonized standards by the Healthcare Information Technology Standards Panel (HITSP). Components that need to be considered during the standards identification and harmonization activities include standardized vocabularies, data elements, datasets, and technical standards that support the information needs and processes of clinical research sponsoring organizations, clinical sites, clinical research and study data management sites and regulatory agencies.

This 2009 Use Case has been developed and with opportunities for review and feedback by interested stakeholders within both the private and public sectors. To facilitate this process, the use cases have been developed in two stages:

A. The **Draft Detailed Use Case** documents all of the events and actions within the use case at a detailed level and facilitates initial discussion with stakeholders; and

B. The **Detailed Use Case** documents all of the events and actions within the use case at a detailed level and reflects the feedback received from stakeholders.

This document is the Detailed Use Case. Feedback received on the Draft Detailed Use Case has been considered and incorporated where applicable into the final Detailed Use Case document. HITSP may reuse standards, where applicable, from standards previously recognized by the Secretary of Health and Human Services, to specify and constrain how standards are to be used to advance interoperability, and to work with standards development organizations to see that gaps in standards are filled.

This Detailed Use Case is divided into the following sections:

- Section 2.0, Introduction and Scope, describes the priority needs identified by one or more AHIC workgroups and includes initial decisions made regarding the scope of the use case;
- Section 3.0, Use Case Stakeholders, describes individuals and organizations that participate in activities related to the use case and its components;
- Section 4.0, Issues and Obstacles, describes issues or obstacles which may need to be resolved in order to achieve the capabilities described in the use case;
- Section 5.0, Use Case Perspectives, describes how the use case combines similar roles (or actors) to describe their common needs and activities. The roles are intended to describe functional roles rather than organizations or physical entities;

- Section 6.0, Use Case Information Flows, describes how various perspectives interact and exchange information within the context of a workflow. Use case information flows provide a context for understanding information needs and are not meant to be prescriptive;
- Section 7.0, Use Case Information Flow Diagrams, provides a greater level of detail for the information flows. Specific events and actions for each perspective and information exchange are presented and discussed. These are also not intended to be prescriptive;
- Section 8.0, Dataset Considerations, identifies specific information opportunities relevant to this use case that may support future standardization and harmonization activities; and
- Section 9.0, Appendix A, the Glossary, provides contextual descriptions of key concepts and terms contained in the detailed use case.

2.0 Introduction and Scope

The Use of Electronic Health Records in Clinical Research: Core Research Data Element Exchange Use Case is based on priorities identified by the American Health Information Community (AHIC) and further guided by the vision and priorities of the multi-stakeholder Clinical Research Value Case Workgroup. The Workgroup has developed a vision document describing approaches for utilizing Electronic Health Record (EHR) data to support clinical research which is available at:

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

The vision has been further developed into a series of incremental steps which focus on one or more ways in which EHR data can support global clinical research activities. For this initial use case, the Workgroup has prioritized the need for harmonized standards to enable exchange of a core set of patient-level clinical information between EHRs and clinical research systems. Future use cases will address other priorities such as identifying candidate subjects for research activities by determining eligibility for particular clinical studies, safety reporting, pharmacogenomics, and compliance reporting.

To guide development of this use case, the Workgroup has also published a "Value Case for the Use of Electronic Health Records in Clinical Research: Processes to Support Core Research Data Element Exchange" available for review at the following location: http://publicaa.ansi.org/sites/apdl/EHR%20Clinical%20Research/Forms/AllItems.aspx. The document describes three value scenarios which are the primary focus of the Clinical Research Use Case:

- Scenario 1: Data exchange from EHR to clinical research sponsor for submission to regulatory, public health, and other agencies
- Scenario 2: Exchange of information from EHR to registries or other databases
- Scenario 3: Exchange of information from EHR in a distributed research network

The needs for harmonized standards to support these three scenarios are described within this use case and are all represented within a combined information flow diagram in section 7.0. Other scenarios, such as identification of subjects for clinical research will be the focus of future use cases. It will be advantageous for standards harmonization and development to be inclusive of all types of clinical research. In addition, it should be comprehensive for all aspects of the clinical research process including, conception, design, execution, communication, and dissemination.

The Use of Electronic Health Records in Clinical Research: Core Research Data Element Exchange Use Case is focused on the electronic exchange of information related to clinical research among sponsors, investigative sites, and regulatory agencies. The focus of this use case is on the harmonization of standards leveraging a core set of widely useful clinical care data from EHR systems to increase the effectiveness and efficiency of clinical research activities. This process will help to foster a continuum between clinical care and clinical research.

The scope of this 2009 Use Case is focused on:

- The ability to communicate study parameters, eligibility information, results, and case report forms within the research community; and
- The ability to exchange a core dataset of de-identified or anonymized information from the EHR for use in clinical research.

Clinical research information exchanged to support the focus of this use case consists of study parameters and protocols, case report forms (CRF), study data, results, and summary reports. To effectively complete clinical research and support communication among sponsors, investigative sites, regulatory agencies, and other reviewers such as government research sponsors and safety monitoring boards, this use case describes some specific information exchanges.

Examples of specific information exchanges:

A. For the purposes of this use case, and in order to clearly define the information flows necessary for the clinical research core data set, the investigative site has been divided into 2 separate functional entities; the study site and the data site. This separation has been defined for illustrative purposes. Most sites do not make this distinction in a physical sense, but instead these two functions tend to be separate. However in many instances, the same personnel may carry out these two functions.

   The use case addresses the potential need for clinical sites to send study information directly to the data site. The clinical site may also send de-identified data to registries. This is a one-way transfer of data from the clinical site to the data site. The only data residing in the EHR regarding the clinical study is an identifier to indicate that the patient is a participant in a clinical study and an identifier for anonymization of the study data. Identifier information would only be available to critical personnel, such as the principal investigator, study coordinator or others with the appropriate permissions. Within the scope of this core dataset use case, information from the clinical study does not flow back to the subject's EHR.

B. The sponsor may send the completed study design to the clinical site and the regulatory agency, as well as the CRF to a centrally hosted server at the data site. They may also transmit subject level data to a reviewer where applicable. The sponsor receives the CRF data back from the data site for tabulation and validation.

   It would be beneficial to sponsors to have electronic communication supporting the transfer of data to investigative sites and regulatory agencies or other reviewers in the case of pharmaceutical studies.

C. Data sites may receive study design and parameter information, information from the clinical site, and centrally hosted CRFs. They may also communicate completed CRF forms and/or bulk data transfers (such as laboratory data) back to the study sponsor.

D. The use case addresses the potential need for regulatory agencies to be informed about clinical study protocols and results.

   Regulatory agencies could benefit from electronic communication supporting: the submission of study design, electronic study registrations, and receiving interim and final reports and audits.

Identification, development, and harmonization of standards to support interoperability associated with clinical research world-wide are addressed in this document. Work with standards and professional organizations, care delivery organizations, and organizations providing information technology services and products to the healthcare industry is needed to support the interoperability needs associated with clinical research. As mentioned in Section 1.0, the needs expressed here have not yet been fully addressed by the national health IT agenda's standardization efforts. Examples of gaps in industry standards are outlined in the upcoming sections of this use case document.

3.0 Use Case Stakeholders

The Stakeholders section provides a listing of all roles, organizations, groups, and entities involved in the processes described in the use case. Rather than providing a definition for each term, a contextual description is provided. This is intended to allow the reader to understand the terms as they are used within the document.

Figure 3-1 Clinical Research Stakeholders Table

Stakeholder	Contextual Description
Academic Research Institution(s)	A college or university associated facility that is endowed to conduct research.
Biobank	A biobank, also known as a biorepository, is a place that collects, stores, processes and distributes biological materials and the data associated with those materials. These may include human biospecimens such as tissue or blood and related clinical information pertaining to the donor of that biospecimen.
Biotechnology Manufacturers	Organizations that design, build, sell, or support the use of biotechnology by consumers to support their health needs with coordinated assistance from clinical and other health support personnel. Biotechnology examples may include adaptive equipment or research laboratory supplies. These organizations are often sponsors of clinical studies.
Central Diagnostics	Organizations which provide laboratory and diagnostic services to study subjects in various settings, which perform and analyze exams as required by the investigative study site. Results of diagnostic tests ordered may include blood or urine tests, X-rays, EKG, etc.
Clinical Research System Vendors	Organizations that develop and provide health information technology solutions for clinical research. These solutions may include applications, data repositories, and web services.
Clinicians	Healthcare personnel with patient care responsibilities, including physicians, advanced practice nurses, physician assistants, nutritionists, nurses, pharmacists and other licensed and credentialed personnel involved in treating study subjects.
Contract Research Organization (CRO)	A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

Stakeholder	Contextual Description
Consumers	Members of the public that include patients as well as caregivers, patient advocates, family members, emergency contacts, and other parties who may be acting for, or in support of, a patient receiving or potentially receiving healthcare services.
Device Manufacturers	Organizations that design, build, sell, or support the use of devices by consumers to support their health needs with coordinated assistance from clinical and other health support personnel. Devices may be regulated medical devices or personal health devices. These organizations are often sponsors of clinical studies.
Electronic Health Record (EHR) System Suppliers	Organizations that provide specific EHR solutions to clinicians and patients such as software applications and software services. These suppliers may include developers, providers, resellers, operators, and others who may provide these or similar capabilities.
Healthcare Payors	Insurers, including health plans, self-insured employer plans, and third party administrators, providing healthcare benefits to enrolled members and reimbursing provider organizations.
Institutional Oversight	Committees whose primary responsibility is to protect the rights and welfare of human research subjects through appropriate review and approvals prior to beginning research. Examples include the Institutional Review Board and Institutional Biosafety Committee.
Investigative Site(s)	Investigative site(s) are the institutions or locations in which clinical research is conducted. These can include clinical sites which may carry out specific clinical care as prescribed by the protocol or study design and study data management sites which are involved in the acquisition, entry, and maintenance of the data generated during the clinical study.
Patient(s)	Members of the public who receive healthcare services.
Patient Advocate	A patient advocate acts as a liaison between the patient and Healthcare Provider. They may speak on behalf of a patient in order to protect their rights and help them obtain needed information and services.
Pharmaceutical Manufacturers	Organizations that design, develop, sell, or support the use of pharmaceuticals by consumers to support their health needs with coordinated assistance from clinical and other health support personnel. These organizations are often sponsors of clinical studies.

Stakeholder	Contextual Description
Public Health Agencies	Federal, state, local, territorial, and tribal government organizations and clinical care personnel that exist to help protect and improve the health of their respective constituents. Examples include but are not limited to the Centers for Disease Control and Prevention, the National Institutes of Health, and local level health departments.
Registries	Organized systems for the collection, storage, retrieval, analysis, and dissemination of research information to support clinical and public health needs. This may include government agencies and professional associations which define, develop, and support research registries such as clinicaltrials.gov. These may also include long-term follow up patient registries, population health registries and disease registries.
Regulatory Agencies	Federal departments within the United States government responsible for the oversight and administration of a specific function. Examples include but are not limited to the Department of Health and Human Services, Food and Drug Administration and the Office for Human Research Protections.
Research Consortia	Networks of researchers working to improve clinical research processes, standards and collaboration within the research community. These may include but are not limited to the Clinical and Translational Science Awards (CTSA), Pharmacogenomics Research Network (PGRN), Cancer Biomedical Informatics Grid (caBIG), and PhenX.
Research Entities	Organizations that are engaged in or support healthcare research including entities performing research, clinical studies, or other research activities (e.g., National Institutes of Health, academic centers).
Research Study Investigator(s)	Members of the medical or scientific community engaged in clinical research. This may include the principal investigator, the study care coordinator and various other personnel involved in clinical research.
Reviewer(s)	Individuals or organizations that review the final tabulated dataset once the study is complete, but have no direct impact on the research data itself and may oversee and approve the initial study protocol and design.

Stakeholder	Contextual Description
Sponsor(s)	The person or organization that takes on ultimate responsibility for the initiation and management (or arranging the initiation and management), reporting the results, and the financing (or arranging the financing) for the study. Examples of sponsors include non-governmental health care measurement organizations, government funding agencies, doctors, medical institutions, foundations, voluntary groups, or pharmaceutical companies.
Study Data Management Professionals	Personnel involved in the acquisition, entry, and maintenance of the data generated during the clinical study. These individuals may be in the employ of the investigative site, placed on site by the sponsoring organization, or working remotely at a CRO or sponsoring organization.
Study Subjects	Members of the public who have volunteered to participate in a clinical study.

4.0 Issues and Obstacles

Realizing the full benefits of health information technology (health IT) is dependent on overcoming a number of issues and obstacles in today's environment. Examples of specific issues and obstacles that are applicable to the Clinical Research Use Case are discussed in this section:

Information interoperability and exchange:

A. There is currently a lack of financial, network, technical, and policy infrastructures to enable information exchange that is secure, consistent, appropriate, reliable, and accurate.

   i. Consequently, research facilities may not have the capabilities to electronically collect, process, and transmit clinical research data in a secure and timely manner.

B. Clinical research data standards are developing independently from certain standards being developed for clinical care data.

   i. Lack of harmonized standards including consistent terminology, nomenclature and semantics used to exchange clinical research data hampers interoperable exchanges of that information. There may be a need to standardize terminology for all clinical research related information and to harmonize these standards with those developing for clinical care.

C. Currently the interface between the EHR and clinical research data can be prone to errors and redundancy.

   i. Working toward harmonizing standards between and among systems and thereby moving the field more towards automation can help make this process more efficient and effective. This may also help reduce study cycle time.

D. Management of informed consent information and their integration into electronic systems can be quite complex.

   i. Informed consent is intimately tied to clinical research protocols.

   ii. This problem is especially challenging for research involving infants, children, and incompetent adults (e.g., trauma victims, cognitively impaired elderly, and comatose study subjects).

E. There may be business-level agreements between health care and/or other organizations for data sharing and use which need unique solutions for the security of protected health information.

   i. Managing these new types of data sharing arrangements may create barriers for acceptance and utilization of clinical research standards.

F. There is a wide variety of modes of research and medical specialties involved in clinical studies making standards difficult to identify.

   i. Because of the variations in the modes of research being performed such as regulated clinical studies, prospective clinical studies, retrospective, or epidemiologic studies there is a need to identify a core set of data standards that can service all types of research in many medical specialties.

G. There are differences among standards developing organizations around healthcare data standards and how they are designed and implemented. These differences may hinder the efforts of HITSP to harmonize global clinical research data standards with healthcare data standards. There are also proprietary standards for clinical research within certain organizations.

   i. There is an ongoing project within Health Level Seven (HL7), sponsored by both the Clinical Data Interchange Standards Consortium (CDISC) and the Food and Drug Administration (FDA), to develop HL7 version 3 messages for structured study information. This includes the HL7 Study Design message for structured protocol information, the HL7 Study Participation message to capture all entities involved in an investigation. This project is also evaluating the use of existing HL7 artifacts (e.g. the HL7 Individual Case Safety Report and HL7 Care Record) to support additional clinical research data needs in a format that is entirely based on the HL7 Reference Information Model. Currently, most EHRs do not support version 3 messages.

   ii. There are various standards and processes involved with the development of clinical research study protocol, study design, and the execution of the study, communication of study status, and dissemination of results. Although these processes are not specifically addressed in this document, they may be addressed in a future use case.

Confidentiality, privacy, security, and data access:

H. Participation in clinical research may be hampered by issues surrounding patient confidentiality and privacy

   i. Consumers fear the loss of privacy protection and unfair consequences (e.g., denial of health insurance or increased premiums) through improper disclosure of family history, disease risk, and predisposition information unless appropriate policies are put in place.

ii. Specific rules may need to be put in place defining who may access and/or view patient related data, particularly when reported from the clinical care EHR.

iii. Systems must comply with all relevant regulations governing confidentiality and privacy such as the Health Insurance Portability and Accountability Act (HIPAA).

iv. In some situations there may be an advantage to sending research generated clinical data back to the patient's EHR. However, this concept may be difficult to implement while maintaining strict patient confidentiality as it relates to clinical study participation.

v. Certificates of confidentiality (COCs), an agreement that addresses protections of researchers from compulsory disclosure of identifying information about their subjects that may be utilized on a wider scale as clinical care systems and clinical research systems are harmonized through standards. While institutional review board (IRB) review and informed consent procedures are mandatory processes to protect human subjects, actions undertaken by investigators and attachment of COCs are voluntary.

I. There may be secondary uses of clinical research information that are not directly addressed by current privacy agreements.

i. Secondary use of data may violate patient privacy and confidentiality. Privacy and confidentiality protections need to be put in place before data access can be automated.

Regulatory Compliance

J. 21 CFR Part 11 states several requirements for electronic systems that may be used in clinical research settings. These requirements must be met in order for systems to exchange information with transactional clinical care systems (i.e. electronic medical record information system).

K. All federally funded clinical research must comply with 45 CFR 46 regulations, including studies which are not regulated by the FDA. These regulations allow for protection of all human research subjects.

L. Most clinical studies, including studies which may not be covered by 21 CFR Part 11 and 45 CFR 46 regulations, must be approved by an IRB. The IRB may be associated with the investigative institution, or may be an outside board contracted by those institutions.

M. 45 CFR 46 regulations require that clinical research documents are presented in the language spoken by and at the appropriate health literacy level for the study subject. Also, individuals who are visually impaired must be given consent documents that meet the 508 compliance regulations for disabled persons.

N. Systems will need to be aware of certain high level regulations such as the HITECH Act, The Title 42, Public Health of the 42 C.F.R. part 52—Grants for Research Projects.

5.0 Use Case Perspectives

The 2009 Clinical Research Use Case describes the flow of information from the initial design of the study, through the clinical care EHR system, the research or study database and if necessary to the appropriate regulatory or reviewing agency. Several perspectives have been identified which contribute to the workflow leading to the exchange of this information. Each perspective is described below:

Sponsoring Organizations

Sponsoring individuals or organizations are responsible for initiation, management, and financing of a clinical study. The sponsor may be a large pharmaceutical, medical device, or biotechnology organization, an academic institution, or a principal investigator or study chair depending on the context of the study. The sponsor is responsible for the study design, protocol development, and all activities related to data, including data entry form development, data acquisition and management, and analysis. The sponsor may choose to contract out any or all of these activities to a Clinical (or contract) Research Organization (CRO) who would carry out these activities under the auspices of the sponsor.

Investigative Site(s)

The investigative site (or sites in the case of multi-site studies) is the institution or location in which the clinical research is conducted. For the purposes of this Use Case, the personnel have been separated into two categories: those carrying out clinical care during the study, and those carrying out data management tasks. In certain instances, there is little or no distinction between these two functions and they are often carried out by the same individuals.

- **Clinical Care (EHR System) Users**

  Clinical care personnel include the principal investigator, physicians from any specialty, nurse care coordinators, nurse practitioners, physician assistants, laboratory specialists, pharmacists, and any other personnel delivering routine or specific clinical care as prescribed by the protocol or study design.

- **Study Data Management System Users**

  Personnel involved in the acquisition, entry, and maintenance of the data generated during the clinical study. These individuals may be in the employ of the investigative site, or may be placed on site by the sponsoring organization. This activity may be carried out by a CRO contracted by the sponsor.

Reviewers

For the purposes of this Use Case, “Reviewers” are referred to as individuals or organizations that review the final tabulated dataset once the study is complete, but have no direct impact on the research data itself and may oversee and approve the initial study protocol and design. Examples of institutions that perform these actions are: National Institutes of Health (NIH), Food and Drug Administration (FDA), National Cancer Institute (NCI), National Center for Research Resources (NCRR) and other organizations with similar missions. The National Library of Medicine (NLM) and other such organizations will receive information on clinical studies for the purpose of study tracking/registration and from downstream databases and possible registries.

In the specific case of controlled clinical studies conducted in the United States, FDA oversees all aspects of the study from initial protocol submission through final approval of the drug or device under study. The FDA must approve products for use in the U.S. even if the research is done elsewhere. The FDA advises that data be submitted in a standardized format in order to facilitate timely review. Regulatory bodies in countries other than the U.S. may have other guidelines that apply to studies done in their countries. Part of the review process involves auditing the data submitted and a review of the processes used to acquire and analyze those data.

Organizational Databases

Organizational databases exist within organizational firewalls and may house data which have been periodically exchanged with EHR systems from multiple investigative sites in a distributed network. Data may be aggregated prior to being transmitted to organizational databases.

Typically, medical products development companies have organizational databases where they aggregate the data from multiple sites to produce what is submitted to regulatory authorities. Another example is a site which has multiple investigators involved and they may aggregate data before submitting to a central location.

6.0 Use Case Information Flows to Support Exchange of the Core Dataset with the EHR

This information flow describes the workflow and information exchange processes of various types of clinical studies. This includes, but is not limited to the classical prospective clinical study which culminates with submission of data to a reviewer. The information flow also describes retrospective, observational, and epidemiological studies. This Use Case assumes the presence of an EHR at the investigative site or sites.

The sponsor or sponsoring organization develops the protocol and design of the research study in conjunction with a principal investigator (PI).

- The protocol and design is sent to the investigative site. At the investigative site or at the sponsor, the protocol, study design and objectives may be reviewed by an Institutional Review Board (IRB), other Ethics Committee, or safety monitoring group. If there are no objections from the reviewer or reviewing body, the clinical study begins with enrollment of study subjects based on eligibility criteria set by the sponsor in the protocol study design.

- Subjects are identified based upon whether they meet the protocol eligibility criteria.

- Various clinical care activities are performed at the investigative site in accordance with the study design.

- Once study subjects are enrolled in the study, a core set of data may be exchanged (essentially copied) from the clinical EHR system to the CRF.

- Study subjects are assigned a study identification number and the number is entered into the EHR such that all information flowing from the EHR to the CRF is anonymized. Currently, this process may be done either entirely on paper or by various electronic means separate from the EHR. There may be additional specific study-specific data collected and entered into the CRF during the course of the study.

- There are special issues in exchanges of data related to standardized terminology sets that can make compilation of data problematic for certain subspecialties. This data may be from patient clinical care interactions or may come from a central diagnostic center, in the form of laboratory results or diagnostic imaging results. (See: Value Case for the Use of Electronic Health Records in Clinical Research: Processes to Support Core Research Data Element Exchange; Scenario 1: Data extraction from EHR to sponsor for submission to regulatory, public health and other agencies)

For retrospective or epidemiologic studies, there may be information sent to a patient registry or database for various purposes, including outcomes or observational research.

- Data may be exchanged in de-identified or anonymized form from a clinical care EHR system for this purpose and utilized for analysis.
- The core dataset of information being exchanged between the clinical care EHR and the study database is similar in nature to the information exchange described above in a prospective clinical study. (See: Value Case for the Use of Electronic Health Records in Clinical Research: Processes to Support Core Research Data Element Exchange; Scenario 2: Exchange of information from EHR to registries or other databases)

This core dataset may be exchanged between the EHR system and a separate study database in a distributed research network.

- In this instance, data may be exchanged on a periodic basis and aggregated in an organizational database.
- This data may be used for multiple purposes such as observational studies, longitudinal studies or quality measures. (See: Value Case for the Use of Electronic Health Records in Clinical Research: Processes to Support Core Research Data Element Exchange; Scenario 3: Exchange of information from EHR in a distributed research network)

During the course of the study, there may be information exchanged between the clinical study and various monitoring organizations such as an IRB, a Data Safety Management Board (DSMB), an ethics committee, and regulator or funding agencies. This is done to ensure the safety of study subjects and the efficacy of the study design.

- Currently, these information exchanges are primarily done with paper forms or by non-standardized electronic data capture systems.

Results from certain clinical trials must be submitted into clinicaltrials.gov, a National Library of Medicine application. Statisticians at the sponsor or CRO may use research data from a central study data repository to produce reports, tables, figures, and listings. Subject level data may need to be part of a regulatory submission as well.

- Currently, CRF data from certain subjects (such as deaths) is most often submitted to the FDA either on paper, or in PDF format. The current preferred method of receiving data within a regulatory submission at FDA's Center for Drug Evaluation and Research is for aggregated CRF data to be submitted as SAS transport files in CDISC Study Data Tabulation Mode (SDTM) format. At the current time, this is referenced in Final Guidance from the FDA rather than a regulation.

7.0 Information Flow Diagram to Support Exchange of the Core Dataset with the EHR

Figure 7-1. Information Flow Diagram to Support Exchange of the Core Dataset with the EHR

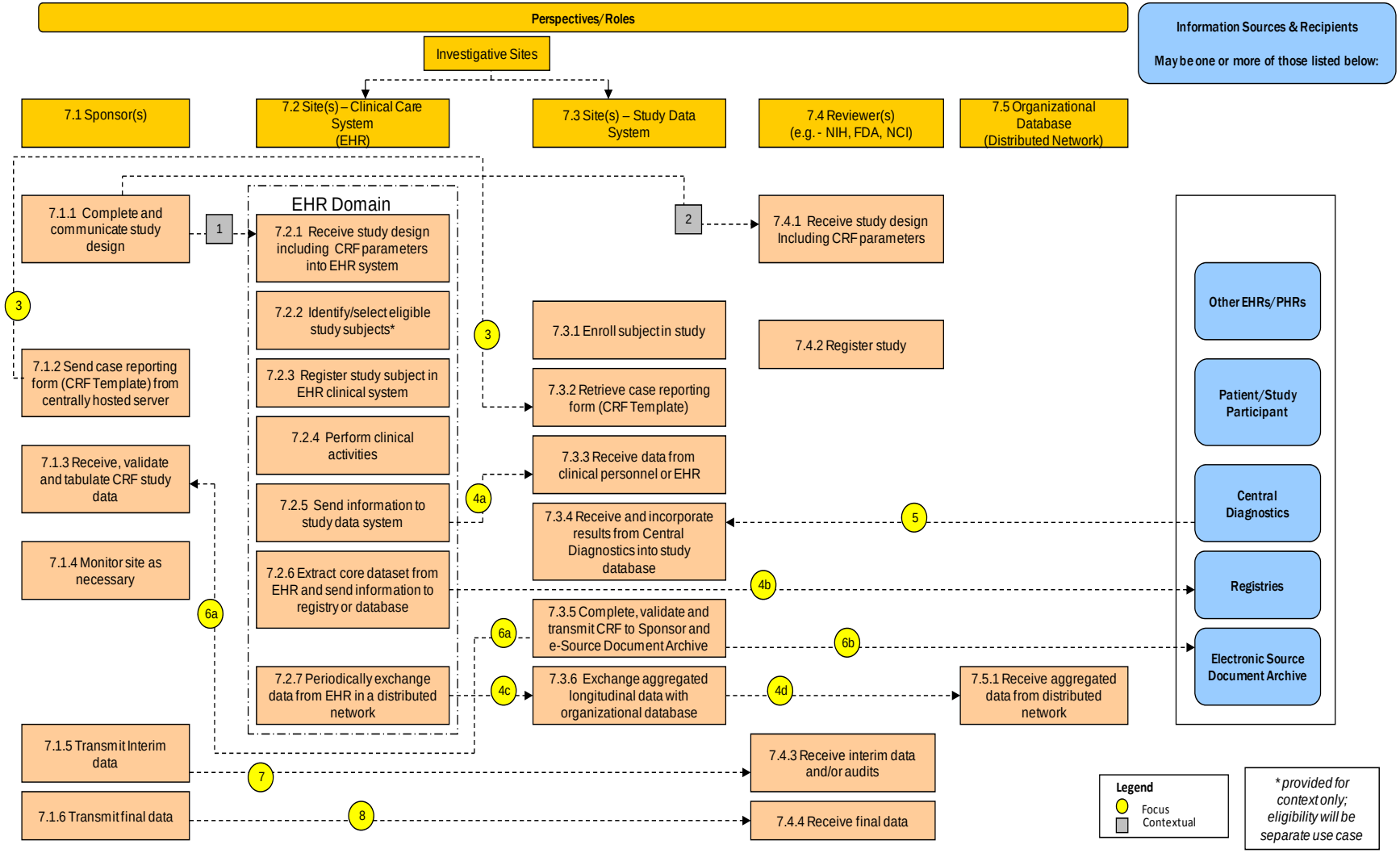

Figure 7-2. Legend for the Information Flows to Support the Exchange of the Core Dataset with the EHR for Clinical Research

1 The IRB approved study design is communicated to the Clinical Care area of the Investigative Site(s). This information may include eligibility criteria. The parameters may be incorporated into the EHR system.

2 The study design is communicated to Reviewer(s).

3 The Case Report Form (CRF) template is sent from a centrally hosted server at the Sponsor to the Study Data Management System.

4a The patient trial information is sent from the Clinical Care System to the Study Data Management System.

4b Information communicated from EHR to registries or other databases.

4c Information is exchanged with the EHR.

4d Aggregated data is sent to the organizational database of the distributed network of site(s).

5 The Study Data Management System receives patient diagnostic results and information from Central Diagnostics.

6a CRF is transmitted from the Study Data Management System to the Sponsor for data validation.

6b CRF is transmitted from the Study Data Management System to the Electronic Source Document Archive.

7 Sponsor sends aggregated data to Reviewer(s).

8 Sponsor transmits application and aggregated data to Reviewer(s).

Legend

Focus: Information exchange that is a primary focus of this use case.

Contextual: Information exchange that is not the primary focus of the use case, but is provided for contextual understanding.

Figure 7-3. Information Flows to Support the Exchange of the Core Dataset with the EHR – Study Sponsor Perspective

Code	Description	Comments
7.1.1	**Event:** Complete and communicate study design	Contextual Flow 1 and Contextual Flow 2.
7.1.1.1	**Action:** Develop study design and protocol.	The sponsor develops the design protocol used to perform the clinical research study. The protocol provides structure to discretely specify eligibility criteria, type of study, doses and/or all other specifics of the clinical work and the feasibility and outcome parameters of the study. This information may include the criteria for eligibility as well as the permissions for who may view this information in the EHR. The sponsor is responsible for defining the target patient population(s) of the particular study. This contextual information flow (Flow 1) is an opportunity for future standards harmonization. There are various standards and processes involved with the development of clinical research such as the authoring of the study conception, design, and the execution of the study, communication, and dissemination of results. Although these processes are not specifically addressed in this document, they may be addressed in a future use case.
7.1.1.2	**Action:** Working with the Principal Investigator.	The sponsor may select the principal investigator and works closely with him/her during the design phase of the clinical study. While recruitment parameters may be set by the sponsor, the PI typically is responsible for the recruitment of study subjects at the investigative site(s).
7.1.1.3	**Action:** Sponsor sends design and protocol to investigative site and Reviewer(s).	Once the design of the study has been developed, the protocols, along with eligibility criteria, likely populations, treatment procedures, and analysis plan are sent to the investigative site. Both the clinical care coordinators and the data managers need to have this information communicated to them. In some instances the protocol design and parameters may be sent directly to the clinical care electronic medical record system which houses the patient's EHR. This is an area which will benefit from harmonizing standards. If the research is a regulated clinical study, this information is sent to the reviewers (Flow 2) where it is analyzed and assessed for likely patient safety and efficacy.

Code	Description	Comments
7.1.2	**Event:** Send case reporting form (CRF Template) from centrally hosted server	Focus Flow 3. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.1.2.1	**Action:** Sponsor sends CRF to the Investigative Site data manager.	The sponsor sends the CRF template to the data manager at the clinical site. The CRF is used to enter data captured during the course of the clinical study. Certain core data may be extracted from the EHR system or as is more common in the current state, entered directly to a separate system with an interface at the investigative site. For observational studies, the CRF may be called the case-control abstract form.
7.1.3	**Event:** Receive, validate and tabulate CRF study data	Focus Flows 6a. These flows conform to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.1.3.1	**Action:** Study data is received from the Investigative Site.	As CRFs are completed, they are sent back to the sponsor. This activity may take place at the investigative site or at a site managed by the sponsor. The CRF may be handled at this stage by a Clinical Research Organization (CRO) contracted by the sponsor.
7.1.3.2	**Action:** Study data is validated.	Once the CRF is received in completed form from the investigative site, the data must be validated and verified. This activity may be handled by a CRO contracted by the sponsor organization. Data validation is a process ensuring that a program operates on clean, correct and useful data. Data must also be verified to be consistent with the source documentation.
7.1.3.3	**Action:** Study data is tabulated.	Once the CRF data is verified and validated, the information may be combined in a study database repository, managed and held by the sponsoring organization for tabulation and/or statistical analysis. This process may involve the integration of various types of data including laboratory data, image data, and other specific forms of data.
7.1.4	**Event:** Monitor site as necessary	

Code	Description	Comments
7.1.4.1	**Action:** Sponsor monitors investigative site.	During the course of the study, the sponsor may contract with a CRO or other group or individual to monitor the ongoing research. The monitor is primarily concerned with the accuracy of the source documents and whether the source documentation matches the CRFs being compiled for the study. Site management must include attention to local factors such as IRB rules and processes and timelines.
7.1.5	**Event:** Transmit interim data	Focus Flow 7. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.1.5.1	**Action:** Interim data is transmitted to a Reviewer.	Interim data may be sent to the Reviewer for various analyses during the study. The Reviewer looks for proper handling of the information as well as a confirmation that study subjects continue to be safe and that the product is showing reasonable efficacy.
7.1.6	**Event:** Transmit final data	Focus Flow 8. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.1.6.1	**Action:** Final data and application for approval is sent to the Reviewer.	The study data is packaged and sent to the Reviewer for final approval. Information may be at both a subject level and/or in aggregated form. The sponsor is responsible for preparing the data for the Reviewer. This may involve statisticians or others involved in the aggregation and analysis of the information. Conflicts of interest should be prospectively identified and managed, including by some form of independent oversight.

Figure 7-4 Information Flows to Support the Exchange of the Core Dataset with the EHR – Investigative Site(s) – Clinical Care System (EHR) Perspective

Code	Description	Comments
7.2.1	**Event:** Receive study design including CRF parameters into EHR system	Contextual Flow 1. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.2.1.1	**Action:** Site receives study design.	The investigative site receives the study design and protocol from the sponsor. In some instances, certain design parameters may be integrated into the EHR system. Both study ID and a means to anonymously identify a patient as a study subject should be integrated into the EHR system. Only staff with appropriate permissions at the investigative site has clearance to view this information. Privacy and confidentiality functionality and the means to enforce it need to be built into the clinical care system. This contextual information flow is an opportunity for future standards harmonization.
7.2.1.2	**Action:** Study sent to Institutional Review Board (IRB) for approval.	The study protocol and design is sent to an IRB for procedural and ethical review. The IRB may be part of the investigative site or may be an independent board contracted by the investigative site. The study may be sent to the IRB by the sponsor or directly from the investigative site. The job of the IRB is to review the proposed study design to ensure that the study is safe for study subjects and that a reasonable degree of efficacy can be expected. If the IRB finds the study to meet these criteria, the sponsor and principal investigator can continue on with the study. The IRB may be part of the organization where the research is taking place or may be contracted by that organization as an external IRB.
7.2.2	**Event:** Identify/select eligible study subjects*	
7.2.2.1	**Action:** Study subjects are selected for the study according to the eligibility criteria set in the study protocol and design.	This section is provided for context only. The steps necessary for determining and selecting eligible study subjects may be the topic of a future use case.

Code	Description	Comments
7.2.3	**Event:** Register study subject in EHR clinical system	
7.2.3.1	**Action: Study subject is enrolled in the EHR clinical system.**	Once eligibility criteria have been met and proper informed consents are signed, a patient is enrolled into the EHR clinical system. The study subject may be interviewed by a clinical care coordinator and be registered into the EHR clinical system as a subject in the specific study by means of a study ID. From this point forward, only personnel with the appropriate permissions may view the study related identifying information in the EHR. Users without these permissions will not be able to see any study information. This is according to individual study design. Only anonymized core dataset information is exchanged from the EHR system.
7.2.4	**Event:** Perform clinical activities	
7.2.4.1	**Action:** Perform all patient activities related to the clinical study.	Over the course of the clinical study, the clinical personnel involved in the research at the investigative site perform various patient related activities according to the study protocol and design. Any information gathered during this period is recorded as source documentation.
7.2.4.2	**Action:** Record all study related information to form the source document.	A core set of information may be extracted from the EHR clinical system, while other information may be study specific and needs to be recorded on an ad hoc basis by the clinical care team into the study database. The percent of information coming from the EHR has been estimated to vary from 5% to 40%. The amount will depend on the specifics of the particular study design. This information in total forms the clinical source document. Any extracted information may need to go through a mapping and conversion process. This process may require recoding (for example, to ICD-9 or SNOMED).
7.2.5	**Event:** Send information to study data system	Focus Flow 4a. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.

Code	Description	Comments
7.2.5.1	**Action:** Source document is sent to the study data system.	Once the source documentation has been completed it is forwarded to the study data system. The information is handled by the personnel charged with this task at the investigative site. In certain cases, this is the PI or the study coordinator, but for large clinical studies, there may be a data manager at the investigative site. This represents one of the key data transactions in prospective clinical studies and/or regulated clinical studies. This is a one way flow of information from the clinical EHR system to a separate study database. Quality assurance measures may be needed at the investigative centers to help avoid common transcription errors and other errors which may cause data to be inaccurate.
7.2.6	**Event:** Extract core dataset from EHR and send information to registry or database	Focus Flow 4b. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.2.6.1	**Action:** Information is sent to registries or other databases.	For retrospective studies, such as epidemiologic studies, the core dataset may be exchanged with the clinical system which houses the EHR and sent to various patient registries or research databases. These systems may be maintained at a single institution or at multiple institutions where they enable aggregation and/or analysis. They may also be maintained by a patient advocacy organization or a government agency (e.g. clinicaltrials.gov). In the future, this exchange may be bi-directional such that information could flow back to the EHR to add to the longitudinal record. This bi-directional type of exchange raises serious issues of privacy and confidentiality which must be handled in accordance with all applicable regulations (e.g. 45 CFR 46).
7.2.7	**Event:** Periodically exchange data from EHR in a distributed network	Focus Flow 4c. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.2.7.1	**Action:** Data is exchanged with the clinical system (EHR) and sent to an intermediate database.	Data may be sent to an intermediate database or data repository where it is aggregated with other datasets over time. This data is gathered from multiple sites around a distributed clinical research network where it is used for longitudinal studies. (see 7.3.5 and 7.5.1)

Figure 7-5. Information Flows to Support the Exchange of the Core Dataset with the EHR– Investigative Site(s) – Study Data Management System Perspective

Code	Description	Comments
7.3.1	**Event:** Enroll subject in study	
7.2.3.1	**Action:** Patient is enrolled in study.	Once eligibility criteria have been met and proper informed consents are signed, a patient is enrolled into the study and becomes a study subject. The study subject may be interviewed by a clinical care coordinator and be registered as a subject in the specific study by means of a study ID. From this point forward, only personnel with the appropriate permissions may view the study related identifying information in the EHR. Users without these permissions will not be able to see any study information. This is according to individual study design. Only anonymized core dataset information is exchanged from the EHR system.
7.2.3.1a	Alternative Action	If these criteria are not met, the patient may not become a study subject or may be removed from the study.
7.3.2	**Event:** Retrieve case reporting form (CRF Template)	Focus Flow 3. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.3.2.1	**Action:** Data manager obtains a CRF template from a server managed by the study sponsor.	The data manager obtains a CRF template from the sponsor's server and sets up a CRF Template for data entry during the study. The CRF may be a paper based form or an electronic form for use with the study database. For most clinical studies, the PI and the study coordinator handle the data at the investigative site.
7.3.3	**Event:** Receive data from clinical personnel or EHR	Focus Flow 4a. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.

Code	Description	Comments
7.3 3.1	**Action:** Data Manager receives the data from the clinical study coordinator and enters the data into a study database.	The data manager receives patient study information from the clinical personnel in the form of a CRF. The data is entered into a study database system. The current method is to keep an independent system, or system link, at the investigative site for the sole purpose of entering the CRF data from the clinical care EHR system. Data is entered into this independent system and later transferred to the sponsor's central server. Some sites and sponsors are moving toward Electronic Data Capture systems (EDC) which may help streamline this process and make it less cumbersome for study subjects and investigators.
7.3.3.2	**Alternative Action:** Data from the EHR is pre-populated on an electronic form with study specific information entered electronically.	In the future, this transaction may take place in a more automated and efficient manner by making the CRF an electronic form which can connect to both the clinical EHR system and the study database in a controlled, anonymized, and confidential manner. One such tool under development is the Retrieve Form for Data Capture (RFD) which connects to the EHR, and pre-populates the form with a core data set, prior to study specific data being entered. This transaction may need to be encrypted for data security and would have to comply with all applicable regulations regarding protected patient health information.
7.3.4	**Event:** Receive and incorporate results from Central Diagnostics into study database	Focus Flow 5. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.3.4.1	**Action:** Diagnostic information is received and incorporated into the study database.	During the course of the study, various kinds of diagnostic information may be required according to the study protocol and design. This information is often obtained at a central laboratory or imaging diagnostic center for consistency of information within the study. Lab results may be sent back to the investigative site or directly to the sponsor and either manually entered into the study database or received in the form of an electronic message through an information exchange. In some instances, if the technology is in place, and the correct permissions are granted, the information should be returned directly to the EHR system and incorporated into the patient's clinical record. In this last instance, the information is subject to all applicable regulations protecting privacy, confidentiality and data access.

Code	Description	Comments
7.3.5	**Event:** Complete, validate and transmit CRF to Sponsor and e-Source Document Archive.	Focus Flows 6a and 6b. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.3.5.1	**Action:** Data is completed and validated.	The data manager completes all data entry into the CRF and may perform validation and verification (these steps may be performed by the sponsor or agent of the sponsor).
7.3.5.2	**Action:** Various safety boards' monitor the study.	During the course of the study there may be various safety boards such as a Data Safety Monitoring Board (DSMB), committees or organizations at the investigative site that monitor the study as it proceeds to ensure that study subjects are not harmed. In addition, they monitor the study to ensure that patient's protected health information remains secure and confidential throughout the course of the study.
7.3.5.3	**Action:** CRF data is transmitted to sponsor.	Once the data entry is complete and validated against the source document, the CRF form is sent back to the sponsor. This may be in paper form or in the form of an eCRF (electronic CRF) for the study visit or patient record. These steps may be completed by the sponsor or agent of the sponsor. The record then becomes a permanent source document for the study meeting the requirements of 21 CFR Part 11.
7.3.5.3a	**Alternative Action:** Additional clarification of transmitted CRF data	After the initial transmission of CRF data to the sponsor, there may be a need for some clarification of some aspect of the information. There may be back and forth communication between the clinical site and the sponsor. This communication is likely to be of an ad hoc nature and is thus not an immediate area for standards development.
7.3.5.4	**Action:** CRF data is transmitted to Electronic Source Document Archive.	Once the data entry is complete and validated against the source document, the CRF data is transmitted to an Electronic Source Document Archive. This archive may be located physically at the investigative site or may be located at a remote location. The record then becomes a permanent source document and is controlled by the investigative site meeting the requirements of 21 CFR 11.

Code	Description	Comments
7.3.6	**Event:** Exchange aggregated longitudinal data from distributed network with organizational database	Focus Flow 4d. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.3.6.1	**Action:** Longitudinal information is aggregated and sent to an organizational database.	In the case of a distributed clinical research network, information is exchanged with EHR systems at multiple sites across the network (see 7.2.7). Data may be aggregated from a single practice with multiple providers or from multiple sites within a network. Core data from the EHR may be anonymized and aggregated over time with other data submissions. This allows for nearly real-time tracking of data across the network.

Figure 7-6. Information Flows to Support the Exchange of the Core Dataset with the EHR – Reviewers Perspective

Code	Description	Comments
7.4.1	**Event:** Receive study design including CRF parameters	Contextual Flow 2. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.4.1.1	**Action:** Reviewer receives a version of the study design and CRF parameters.	The reviewer(s) receive a version of the study protocol and design. This takes place prior to the start of the clinical research. Currently, this information may be sent on paper or electronically in the form of a PDF file.
7.4.2	**Event:** Register study	
7.4.2.1	**Action:** Clinical study is registered with the reviewer.	This step always takes place if the research is a controlled clinical trial but may not always happen in a formalized manner in other types of studies. A controlled study is registered with the Reviewer and given a case number. From this point forward, the study may be monitored by the Reviewer in various ways, including interim reports and/or audits.

Code	Description	Comments
7.4.3	**Event:** Receive interim data and/or audits	Focus Flow 7. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.4.3.1	**Action:** Sponsor sends interim data reports and/or audits to the reviewer.	During the course of the clinical study, the reviewer may request interim reports of data or conduct an audit. The purpose of these interim reports and audits is to monitor the performance of the study with regard to patient safety and efficacy of the product or process under study. The study may be suspended or ceased if there is a concern that safety concerns are not being met or if the product or process is not efficacious. Alternatively, if the treatment is deemed so beneficial that not allowing full access is deemed unethical, then the study may be ended in order to shorten the time to general use.
7.4.3.2	**Action:** Sponsor and reviewer may exchange information regarding the ongoing study.	Situations may arise during an audit or interim report in which the sponsor may need to communicate back to the reviewer to ensure that the correct information is present and all the necessary information has been gathered to ensure the study is proceeding as designed. This communication is likely to be of an ad hoc nature, but is an opportunity for focused communication in the future.
7.4.4	**Event:** Receive final data	Focus Flow 8. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.4.4.1	**Action:** Sponsor sends final data at the end of the clinical study.	When sufficient sample size has been reached and all data has been locked down, tabulated, analyzed, and/or aggregated, the sponsor sends the application for approval to the Reviewer. The Reviewer(s) conducts a thorough evaluation of all the information, and makes a final decision regarding approval of the treatment for routine clinical use. In the case of a controlled clinical trial, this process is performed by the FDA and may be more rigorous and formalized than for non-regulated studies.

Figure 7-7. Information Flows to Support the Exchange of the Core Dataset with the EHR – Organizational Database Perspective

Code	Description	Comments
7.5.1	**Event:** Receive aggregated data from distributed network	Focus Flow 4d. This flow conforms to the data transport, security, privacy and other requirements described in the 2009 Common Data Transport Extension/Gap.
7.5.1.1	**Action:** Aggregated data is received by the organizational database.	As part of the data handling in distributed clinical research networks, data is aggregated and then received at an organizational database which resides within an organizational firewall. Data is maintained here and is available for queries and other uses. Users of different types may have access to this data under very controlled conditions meeting relevant patient protection regulations such as 45 CFR 46.

8.0 Clinical Research Dataset Considerations

This section provides a listing of information types that may be relevant for the scenario previously discussed. The information types shown are not intended to be a comprehensive listing. At this time, there is discussion regarding what might comprise a summary dataset and/or standards for the transfer of appropriate and necessary information to facilitate clinical research.

Datasets are still being developed and expected to be the result of a complementary parallel process involving the various efforts in the industry. The following non-exhaustive information categories and limited examples are for the purposes of addressing the scenarios in this use case. These examples are not intended to be inclusive of all activities in this area.

For Clinical Research, the following data elements may be found in a Case Report Form and a related EHR:

A. Planning and Reporting Requirements
    i. Informed consents
    ii. Eligibility verification
    iii. Study design

B. Subject Demographics
    i. Subject identifier
    ii. Date of birth
    iii. Sex
    iv. Race
    v. Ethnic/cultural background
    vi. Native language
    vii. Date and time collected

C. Prior and Concomitant Medications
    i. Medication
    ii. Indication
    iii. Dose
    iv. Timing of medication
    v. Route
    vi. Rate
    vii. Length of time on medication
    viii. Date and time collected

D. Medical History
    i. Type of history
    ii. Allergies
    iii. Surgeries
    iv. Family history
    v. Diet
    vi. Exercise

vii. Concomitant therapies
viii. Date and time collected

E. Physical Examination
   i. Body system examined
   ii. Results
   iii. Clinical comments
   iv. Date and time collected

F. Substance Use
   i. Type of substance
   ii. Occurrence of use
   iii. Frequency and duration
   iv. Date and time collected

G. Vital Signs
   i. Results and units
   ii. Clinical comments
   iii. Date and time collected

H. Diagnostic Data
   i. Test name
   ii. Test result and units
   iii. Clinical comments
   iv. Date and time collected

I. Adverse Clinical Events
   i. Type of event
   ii. Severity
   iii. Action taken
   iv. Outcome
   v. Date and time collected

9.0 Appendix A: Glossary

These items are included to clarify the intent of this use case. They should not be interpreted as approved terms or definitions but considered as contextual descriptions. There are parallel activities underway to develop specific terminology based on consensus throughout the industry.

Academic Research Institution(s): A college or university associated facility that is endowed to conduct research.

AHIC: American Health Information Community; a federal advisory body chartered in 2005, serving to make recommendations to the Secretary of the U.S. Department of Health and Human Services regarding the development and adoption of health information technology.

Biobank: A biobank, also known as a biorepository, is a place that collects, stores, processes and distributes biological materials and the data associated with those materials. These may include human biospecimens such as tissue or blood and related clinical information pertaining to the donor of that biospecimen.

Biotechnology Manufacturers: Organizations that design, build, sell, or support the use of biotechnology by consumers to support their health needs with coordinated assistance from clinical and other health support personnel. Biotechnology examples may include adaptive equipment or research laboratory supplies. These organizations are often sponsors of clinical studies.

Case Report Form (CRF): A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor for each trial subject. Also a record of clinical study observations and other information that a study protocol designates must be completed for each subject. Note: In common usage, CRF can refer to either a CRF page, which denotes a group of one or more data items linked together for collection and display, or a casebook, which includes the entire group of CRF pages on which a set of clinical study observations and other information can be or have been collected, or the information actually collected by completion of such CRF pages for a subject in a clinical study.

Central Diagnostics: Organizations which provide laboratory and diagnostic services to study subjects in various settings, which perform and analyze exams as required by the investigative study site. Results of diagnostic tests ordered may include blood or urine tests, X-rays, EKG, etc.

Certification Commission for Healthcare Information Technology (CCHIT): is a recognized certification body (RCB) for electronic health records and their networks, and an independent, voluntary, private-sector initiative. CCHIT's mission is to accelerate the adoption of health information technology by creating an efficient, credible, and sustainable certification program.

Clinical Care Personnel: Clinical care personnel include the principal investigator, physicians from any specialty, nurse care coordinators, nurse practitioners, physician

assistants, laboratory specialists, pharmacists and any other personnel delivering routine or specific clinical care as prescribed by the protocol or study design.

Clinical Care (EHR System) Users: Clinical care personnel include the principal investigator, physicians from any specialty, nurse care coordinators, nurse practitioners, physician assistants, laboratory specialists, pharmacists and any other personnel delivering routine or specific clinical care as prescribed by the protocol or study design.

Clinical Research System Vendors: Organizations that develop and provide health information technology solutions for clinical research. These solutions may include applications, data repositories, and web services.

Clinicians: Healthcare providers with patient care responsibilities, including physicians, advanced practice nurses, physician assistants, nurses, psychologists, pharmacists, and other licensed and credentialed personnel involved in treating study subjects.

Consumers: Members of the public that include patients as well as caregivers, patient advocates, surrogates, family members, and other parties who may be acting for, or in support of, a patient receiving or potentially receiving healthcare services.

Contract Research Organization (CRO): A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

Department of Health and Human Services (HHS): The United States federal agency responsible for protecting the health of the nation and providing essential human services with the assistance of its operating divisions that include: Administration for Children and Families (ACF), Administration on Aging (AOA), Agency for Healthcare Research and Quality (AHRQ), Agency for Toxic Substances and Disease Registry (ATSDR), Centers for Disease Control and Prevention (CDC), Centers for Medicare & Medicaid Services (CMS), Food and Drug Administration (FDA), Health Resources and Services Administration (HRSA), Indian Health Services (IHS), National Institutes of Health (NIH), Program Support Center (PSC), and Substance Abuse and Mental Health Services Administration (SAMHSA).

Device Manufacturers: Organizations that design, build, sell, or support the use of devices by consumers to support their health needs with coordinated assistance from clinical and other health support personnel. Devices may be regulated medical devices or personal health devices. These organizations are often sponsors of clinical studies.

Electronic Data Capture (EDC): a computerized system designed for the collection of clinical data in electronic format for use in clinical trials. Typically, EDC systems provide a graphical user interface component for data entry, a validation component to check user data, and a reporting tool for analysis of the collected data.

Electronic Health Record (EHR): The electronic health record is a longitudinal electronic record of patient health information generated in one or more encounters in any care delivery setting. This information may include patient demographics, progress notes,

problems, medications, vital signs, past medical history, immunizations, laboratory information, and radiology reports.

Electronic Health Record (EHR) System Suppliers: Organizations which provide specific EHR and/or PHR solutions to clinicians, consumers, and patients such as software applications and software services. These suppliers may include developers, providers, resellers, operators, and others who may provide these or similar capabilities.

Healthcare Entities: Organizations that are engaged in or support the delivery of healthcare. These organizations could include hospitals, ambulatory clinics, long-term care facilities, community-based healthcare organizations, employers/occupational health programs, school health programs, dental clinics, psychology clinics, care delivery organizations, pharmacies, home health agencies, hospice care providers, and other healthcare facilities.

Healthcare Payors: Insurers, including health plans, self-insured employer plans, and third party administrators, providing healthcare benefits to enrolled members and reimbursing provider organizations.

HIPAA: Enacted by Congress in 1996, the Health Insurance Portability and Accountability Act (HIPAA, Title II) required the Department of Health and Human Services (HHS) to establish national standards for electronic health care transactions and national identifiers for providers, health plans, and employers. It also addressed the security and privacy of health data. As the industry adopts these standards for the efficiency and effectiveness of the nation's health care system will improve the use of electronic data interchange.

HITSP: The American National Standards Institute (ANSI) Healthcare Information Technology Standards Panel; a body created in 2005 in an effort to promote interoperability and harmonization of healthcare information technology through standards that would serve as a cooperative partnership between the public and private sectors.

Informatician(s): Individuals practicing information management and the technology of information storage, retrieval and transmission.

Informed Consent: An ongoing process that provides the subject with explanations that will help in making educated decisions about whether to begin or continue participating in a trial. Informed consent is an ongoing, interactive process rather than a onetime information session.

Institutional Oversight: Committees whose primary responsibility is to protect the rights and welfare of human research participants through appropriate review and approvals prior to beginning research. Examples include the Institutional Review Board and Institutional Biosafety Committee.

Investigative Sites: Investigative site(s) are the institutions or locations in which clinical research is conducted. These may include clinical sites which may carry out specific clinical care as prescribed by the protocol or study design and data management sites which are involved in the acquisition, entry, and maintenance of the data generated during the clinical study.

Knowledge Suppliers: Entities that use data, vocabulary, technology, and/or industry standards to provide information and tools to entities delivering health care.

Patient(s): Members of the public who receive healthcare services.

Patient Advocate: A Patient Advocate acts as a liaison between the patient and Healthcare Provider. They may speak on behalf of a patient in order to protect their rights and help them obtain needed information and services.

Pharmaceutical Manufacturers: Organizations that design, develop, sell, or support the use of pharmaceuticals by consumers to support their health needs with coordinated assistance from clinical and other health support personnel. These organizations are often sponsors of clinical studies.

Providers: The healthcare clinicians within healthcare delivery organizations with direct patient interaction in the delivery of care, including physicians, nurses, psychologists, and other clinicians. This can also refer to healthcare delivery organizations.

Public Health Agencies: Federal, state, local, territorial, and tribal government organizations and clinical care personnel that exist to help protect and improve the health of their respective constituents. Examples include but are not limited to the Centers for Disease Control and Prevention, the National Institutes of Health, and local level health departments.

Registries: Organized systems for the collection, storage, retrieval, analysis, and dissemination of research information to support health needs. This may include government agencies and professional associations which define, develop, and support research registries such as clinicaltrials.gov. These may also include long-term follow up patient registries and disease registries.

Regulatory Agencies: Federal departments within the United States government responsible for the oversight and administration of a specific function. Examples include the Department of Health and Human Services, Food and Drug Administration and the Office for Human Research Protections.

Research Consortia: Networks of researchers working to improve clinical research processes, standards and collaboration within the research community. These may include but are not limited to the Clinical and Translational Science Awards (CTSA), Pharmacogenomics Research Network (PGRN), Cancer Biomedical Informatics Grid (caBIG), and PhenX.

Research Entities: Organizations that are engaged in or support healthcare research including entities performing research, clinical studies, or other research activities. Examples include the National Institutes of Health and academic centers.

Research Study Investigators: Members of the medical or scientific community engaged in clinical research. This may include the principal investigator, the study care coordinator and various other personnel involved in clinical research.

Reviewer(s): Individuals or organizations that review the final tabulated dataset once the study is complete, but have no direct impact on the research data itself and may oversee and approve the initial study protocol and design.

Sponsor(s): The person or organization that takes on ultimate responsibility for the initiation and management (or arranging the initiation and management) of, and the financing (or arranging the financing) for the study. Examples of sponsors include non-governmental health care measurement organizations, government funding agencies, doctors, medical institutions, foundations, voluntary groups, or pharmaceutical companies.

Standards: Criterion or specification established by authority or consensus for measuring performance. Also, quality specifying conventions that support interchange of common materials and information. Types of standards may include data, format, legal, quality, transport, date/time, and security/privacy.

Study Data Management Professionals: Personnel involved in the acquisition, entry, and maintenance of the data generated during the clinical study. These individuals may be in the employ of the investigative site, placed on site by the sponsoring organization, or working remotely at a CRO or sponsoring organization.

Study Data Management System: A system used by the sponsor or contracted CRO to compile, integrate and provide extractions of data for analysis.

Study Data Management System Users: Personnel involved in the acquisition, entry, and maintenance of the data generated during the clinical study. These individuals may be in the employ of the investigative site, or may be placed on site by the sponsoring organization. This activity may be carried out by a CRO contracted by the sponsor.

Study Subjects: Members of the public who have volunteered to participate in a clinical study.