

HITSP Clinical Research Interoperability Specification

HITSP/IS158



Healthcare Information Technology Standards Panel

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1.0 INTRODUCTION

This Healthcare Information Technology Standards Panel (HITSP) document is divided into Requirements, Design and Capabilities sections which may be used by analysts, architects and implementers. Analysts might use this document to refer to the requirements of a particular Harmonization Request. Architects and system implementers might refer to this document as the top level architectural specification for a system design while software developers will use the Interoperability Specification as a source of requirements for interoperable information exchange.

The following table details specific sections of this Interoperability Specification template and how specific sections of this document are targeted to specific readers. Each of the stakeholders listed in this table are more fully defined in a separate appendix. This table is provided as an aid to readers to assist with identifying specific areas of focus. Readers are encouraged to review all sections of this document to further their understanding of HITSP's work.

Table 1-1 Reader's Guide for Interoperability Specification

Document Section	Section Number	Intended Audience	Information Contained
Section 2.0 Requirements	2.1 Synopsis of Requirements	Policy Managers Policy Analysts Executive Leadership	Used to provide an overview (using a scenario-based approach) of the requirements applicable to this document. Readers should start here to learn more about what specific requirements this Interoperability Specification is intended to address
	2.2 - 2.4 Scenarios	Program Managers Policy Analysts Executive Leadership	Each of the scenarios specific to the Interoperability Specification are outlined and described using a HITSP concept known as an Information Exchange Requirement (IER). HITSP uses IER's to outline requirements for HITSP work products
	2.5 System Description	Architects Business Analysts Policy Analysts Program Managers	The systems assigned to the system roles (as defined in the HITSP Capabilities used by this Interoperability Specification) are identified and described here. Readers can learn which systems have been included as part of this HITSP Interoperability Specification
Section 3.0 Design Specification	3.1 Capabilities Used	Architects Business Analysts Development Team	For each Information Exchange Requirement (IER) identified in Section 2.0, a corresponding HITSP Capability is associated and mapped. A reader can review how specific HITSP Capabilities meet information exchange needs. A diagram is also provided to show the interchange of data among systems identified in this Interoperability Specification
	3.2 Capability Orchestration	Architects Development Team	The core of the design in the Interoperability Specification is documented here. This solution shows orchestration of Capabilities to meet the specific Information Exchange Requirements (IER) in Section 3.1. The design also identifies conditions and constraints, as well as any content subsets specific to the solution
Section 4.0 Capability Gaps	4.0 Capability Gaps	Business Analysts Development Team Architects	Gaps specific to Capabilities used as part of this Interoperability Specification are reviewed in this section to determine why specific information exchange requirements may not yet be met or defined. Readers should check this section to track the progress of gap resolution
Section 5.0 Appendix	5.1 Provisional Exchange Content Description	Architects	Supporting information is provided for HITSP exchange content that is identified as provisional (due to gaps identified in the previous section)
	5.2 Provisional Data Requirements	Architects	Supporting information is provided for HITSP data requirements that are associated with provisional exchange content identified in Section 5.1
	5.3 Harmonization Request Traceability	Architects Business Analysts	A complete mapping of information exchange requirements to functional requirements is provided in this section. Readers can trace IER's to underlying Harmonization Request events and actions (in those instances where a Use Case exists) or to functional requirements defined as part of



Document Section	Section Number	Intended Audience	Information Contained
			an official standards Harmonization Request

1.1 INTEROPERABILITY SPECIFICATION OVERVIEW

The Use of Electronic Health Records in Clinical Research: Core Research Data Element Exchange Use Case focuses on ways in which EHR data can support global clinical research activities, with immediate reference to the U.S. Realm. This Use Case came forward as an independently funded effort of ONC and CDISC. AHIC expressed interest in clinical research early on, but did not develop a Use Case, a situation remedied by the efforts of CDISC and ONC. Specifically, this Use Case focuses on exchange of a core set of patient-level clinical information between EHRs and clinical research systems. The key interfaces in this Use Case are the research sponsors, investigative sites (any healthcare site that is participating in a clinical research study), and regulatory agencies. The goal of this Interoperability Specification is to identify appropriate standards for the exchange of information inclusive of all types of clinical research. The scope of this effort is on:

- The ability to communicate information about particular study participants: eligibility information, results, and case report form data
- The ability to exchange a core dataset of pseudonymized or anonymized information from the EHR to a research system for use in clinical research

The Clinical Research Interoperability Specification follows the Use Case closely, and is informed by the prior work of HL7, CDISC, and IHE; testing and demonstrations of EHR and clinical research cooperation at four Connectathons and three HIMSS Interoperability Showcase, two real world implementations, and the HL7 EHR Clinical Research Functional Profile developed by the EHR-CR collaborative of Pharmaceutical Research and Manufacturers of America (PhRMA) and eClinical Forum. It also draws on existing HITSP constructs and addresses gaps with emerging standards and integration profiles. This Interoperability Specification draws upon the IHE profile Clinical Research Document (CRD) that relies in turn on CDISC's Clinical Data Acquisition Standards Harmonization (CDASH) specification of data elements known to be of interest to clinical research studies. The CRD specification enables any EHR to export a well specified set of data elements, initially exchanged with the Continuity of Care Document that can be transformed for use in clinical research studies. In operation, this will be accomplished in a workflow in which any of these data elements will automatically populate a case report form that will then surface within the EHR for review and completion. The case report form will also require study specific data which will not be available in the EHR. Data required by the study which the EHR cannot provide will be entered by the site investigator or designee, who are assumed as users of the EHR, at the time of the study visit, using the Capabilities of HITSP/TP50 and the IHE profile Retrieve Form for Data Capture (RFD). The aspect of clinical research that requires using a forms-based approach based on RFD (HITSP/TP50) rather than using direct data extraction is shared with the closely allied Interoperability Specifications for Quality (HITSP/IS06) and Public Health Case Reporting (HITSP/IS11). The use of the data archive function, in particular, is intended to meet the needs of 21 CFR part 11. The pre-population data along with the specific research data not originating in the EHR are preserved in the forms archiver as source information. This archive step can be done independent of the EHR, or within the EHR, but in the latter case only if the EHR takes steps to be validated as 21 CFR 11 compliant. This forms approach brings with it serious challenges of confidentiality and privacy. In the case of protocol driven sponsored research, Use Case scenario one, it is not sufficient for EHRs to export a CRD to the research system without regard for the limitations of the sponsor's protocol. The workflow is complicated by the requirement that only those data required by the protocol be delivered to the sponsor's system, and the Interoperability Specification takes this requirement into account as one of the policy variants required.

The registry scenario, designated as scenario two, has fewer restrictions on privacy and confidentiality since the patient identity can usually be known to the registry database. This range of policy requirements around privacy and confidentiality will be addressed by articulating taxonomy of policy configurations that can be addressed by the full armamentarium of Security and Privacy constructs.



The research network scenario positions a data aggregator, the research network system, between the participating healthcare sites and the research system, the EDC.

1.2 DOCUMENT SCOPE

The scope of the document is U.S. realm only. It covers clinical research in all its forms as it interoperates with healthcare systems, particularly EHRs. The specification spans two industries, healthcare and clinical research, and incorporates standards from healthcare (HL7 and IHE) and research (CDISC). The design leverages existing HITSP constructs and communication methodologies where applicable, and lays out new constructs as needed. The design also leverages the current players in the clinical research industry such as Electronic Data Capture (EDC) systems and research registries.

1.3 COPYRIGHT PERMISSIONS

COPYRIGHT NOTICE

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1.4 REFERENCE DOCUMENT

A list of key reference documents and background material is provided in the table below. HITSP-maintained reference documents can be retrieved from the [HITSP Web Site](#).

Table 1-2 Reference Documents

Reference Document	Document Description
HITSP Acronyms List	Lists and defines the acronyms used in this document
HITSP Glossary	Provides definitions for relevant terms used by HITSP documents
TN900 – Security and Privacy	TN900 is a reference document that provides the overall context for use of the HITSP Security and Privacy constructs
TN903 – Data Architecture	TN903 is a reference document that provides the overall context for use of the HITSP Data Architecture constructs
TN904 – Harmonization Framework and Exchange Architecture	TN904 is a reference document that provides the overall context for use of the HITSP Harmonization Framework and Exchange Architecture

1.5 CONFORMANCE

This section describes the conformance criteria, which are objective statements of requirements that can be used to determine if a specific behavior, function, interface, or code set has been implemented correctly.

1.5.1 CONFORMANCE CRITERIA

For an implementation to claim conformance to a HITSP Interoperability Specification, it must be implemented in its entirety or within a limited scope or subset as defined within the Interoperability Specification, its associated construct specifications, as well as conformance criteria from the selected base and composite standards. A conformant system must be constrained as specified in this Interoperability Specification, and implement all of the required interfaces within the scope, subset or implementation options as described.



1.5.2 CONFORMANCE SCOPING, SUBSETTING AND OPTIONS

HITSP may define the permissibility for system scoping, subsetting or implementation options by which the specification may be implemented in a limited manner. The selected scope, subset or options shall specifically be stated, and implementations must include all requirements within the selected scope, subset or options to claim conformance.

For this Interoperability Specification, conformance may be declared by a participating system for any Capability provided that all declared constraints, conditions and requirements imposed by the Capability and its referenced HITSP constructs are satisfied.

1.5.3 TEST METHODS

HITSP relies on the conformance test methods, test tools and other test-related material produced by, or under the auspices, of standards developers, profiling organizations and implementation guide producers as part of its collaborative implementation testing effort. Efforts to produce conformance test methods, tools, etc. may be internal to the organization or provided by an external organization.

An [HIT Implementation Testing and Support](#) Web Site has been developed in collaboration with HITSP, the National Institute of Standards and Testing (NIST), the Certification Commission for Healthcare Information Technology (CCHIT), and the Office of the National Coordinator for Health Information Technology (ONC) to advance conformance and interoperability testing Capabilities. This Web Site provides HIT implementers with the necessary resources to support and test their implementation of standards-based health systems.



2.0 REQUIREMENTS ANALYSIS

Section 2.0 identifies the requirements from the Use Case for which information exchanges are necessary. The following table details how this section and other sections of the document are targeted to specific readers. Each of the stakeholders listed in this table are more fully defined in a separate appendix. This table is provided as an aid to readers to assist with identifying specific areas of focus. Readers are encouraged to review all sections of this document to further their understanding of HITSP's work.

Table 2-1 Reader's Guide for Section 2.0

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	2.2 – 2.4 Scenarios	Program Managers Policy Analysts Executive Leadership	Each of the scenarios specific to the Interoperability Specification are outlined and described using a HITSP concept known as an Information Exchange Requirement (IER). HITSP uses IER's to outline requirements for HITSP work products
	2.5 System Description	Architects Business Analysts Policy Analysts Program Managers	The systems assigned to the system roles (as defined in the Capabilities used by this Interoperability Specification) are identified and described here. Readers can learn which systems have been included as part of this Interoperability Specification

2.1 SYNOPSIS OF REQUIREMENTS

The following table describes the information exchange requirements needed to accomplish the Use Case for which information exchange is necessary.

Table 2-2 Description of Information Exchange Requirements

Information Exchange Requirement Number (IER)	Description
IS158-IER1	Scenarios 1 and 3: EHR or research network system sends redacted patient header data (DR1, DR2, DR3, DR13) to EDC. Reference action 7.2.3.1. Confidentiality and consent policy configuration determine the specific data elements to be redacted
IS158-IER2	Scenario 1 and 3: EDC sends pseudonymous subject identifier to research network system or site EHR. Reference action 7.3.1.1
IS158-IER3	Scenarios 1 and 3: EHR or research network system sends redacted clinical research document to EDC. Reference action 7.2.5.1 part 1, 7.2.7.1, 7.3.6.1, IER8. Research protocol and confidentiality policy determines data elements to be redacted
IS158-IER4	Scenarios 1 and 3: EDC returns pre-populated CRD to EHR or Research Network system. Ref action 7.3.3.2 part 1, IER9
IS158-IER5	Scenarios 1 and 3: EHR or research network system sends completed case report form to EDC. Reference action 7.2.5.1 part 2, 7.3.3.2 part 2, IER10
IS158-IER6	Scenario 2: EHR sends patient information (DR1, DR2, DR3, DR13) to registry. Reference action 7.2.3.1, IER1
IS158-IER7	Scenario 2: Registry system sends subject identifier to EHR. Reference action 7.3.1.1, IER2
IS158-IER8	Scenario 2: EHR sends clinical research document to registry system. Reference action 7.2.6.1 part 1, IER3
IS158-IER9	Scenario 2: Registry system returns partially pre-populated registry form to EHR. Ref action 7.3.3.2 part 1, IER9
IS158-IER10	Scenario 2: EHR sends completed data form to Registry System. Reference 7.2.6.1 part 2, 7.3.3.2 part2, IHE5
IS158-IER11	Scenario 1, 2, and 3: EHR or research network system sends document (CCD, CRD) to electronic source document archive. Ref. action 7.3.5.4



Information Exchange Requirement Number (IER)	Description
IS158-IER12	Scenario 1 and 3: Receive laboratory information from central diagnostic facilities. Ref action 7.3.4.1
IS158-IER13	Scenario 1 and 3: Receive image information from central diagnostic facilities. Ref action 7.3.4.1

Table 2-3 lists and describes the major subdivisions of a Harmonization Request, called Scenarios.

The Clinical Research Harmonization Request comprises three scenarios for the exchange of electronic health record data in support of research. In all three scenarios listed below, best practices and regulatory requirements of patient privacy and data security apply, but the scenarios have different privacy requirements. For example, scenario one requires that all patient data are pseudonymized whereas scenario two allows fully identified data. Table 2-3 lists and describes the major subdivisions of a Harmonization Request, called Scenarios.

Table 2-3 Description of Scenarios

Scenario Name	Scenario Description
Protocol-driven Sponsored Research	This scenario describes six processes that result in submission of clinical data to a sponsoring organization as dictated by a sponsor's protocol. It contains most of the data elements of interest
Registry Reporting	This scenario varies only slightly from the Sponsored Research Scenario, and describes the exchange of clinical data with a research registry or other related databases
Research Network	This third scenario, in which data originate in a networked environment, merely changes the mode of origination

2.2 PROTOCOL-DRIVEN SPONSORED RESEARCH SCENARIO

This scenario describes six processes, defined by the Use Case, that result in submission of data from an EHR to a clinical research sponsor for ultimate submission to regulatory, public health and other agencies. The data requirements are specified in the sponsor's research protocol. Note that, since each protocol has unique data requirements, exact and complete specification of data cannot be accomplished. The best that can be done is to specify best practice data elements that are likely to be required by all protocols, and to provide for collection of ad hoc data that cannot be specified in advance. The processes are described below.

Identification, Screening, and Enrollment. The EHR will notify the Clinical Research Organization (CRO) or Sponsor when a subject is identified as a candidate for a study (i.e. deemed eligible per the research protocol). The subject should receive a subject identifier at enrollment for that study 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). Verification of the identity of the subject of the study is the responsibility of the site investigator.

Data Collection. A case report form (CRF) for a clinical protocol is pre-populated with data identified within the Electronic Health Record (EHR). Core research data elements, the basics required for every study are identified by the Clinical Data Acquisition Standards Harmonization (CDASH). Following confirmation by the investigator or study coordinator that these data are correct and accurate, they can be exported from the EHR into the research repository which is housed by a research system vendor, CRO, or study sponsor, via an Electronic Data Capture (EDC) system or other clinical research system. The electronic source data, including audit trail, are maintained in the EHR at the investigative site or in an appropriate archive format at the site or at a third party under contract to the site. Core dataset information present in the EHR would be available to the research repository. Additional data, specific to the clinical study, may be collected and sent to the research repository in addition to populating the EHR as appropriate (to retain the electronic source record). This would streamline the workflow for the investigative site. The associated terminology would be mapped between EHR and research systems.



Source Data Verification. Source Data Verification ensures that the subject's data have been captured appropriately. Source documents are created by exporting pre-population data from the EHR to the EDC system, and by the completion of missing data elements by the EHR user, under the authority of the site investigator. These resulting source documents will be available either in the EHR or in the electronic source archive. This document provides an exact record of the source of the pre-population, including identification of data NOT selected for pre-population.

Institutional Review Board (IRB) and Data Safety Management Boards (DSMB). Information may need to be exchanged between the clinical study and DSMB, IRB, ethics committees, regulators or government funding agencies to ensure the safety of subjects in the study, as specified in the research protocol. The Capability to send electronic data to the DSMB for review 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 for de-identified information to be warehoused for future analyses. Rigorous data definitions facilitate pooling data from multiple studies, pursuant to privacy regulation and best practice. At the conclusion of the trial, results should be published in a trial registry 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 research repository 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.

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.

2.2.1 INFORMATION EXCHANGE REQUIREMENTS FOR PROTOCOL DRIVEN SPONSORED RESEARCH

Table 2-4 Protocol-driven Sponsored Research Information Exchange Requirements summarizes the relationship between the Exchange Action, Exchange Content, and the Initiating and Responding System(s) along with Exchange Attributes.

Table 2-4 Protocol-driven Sponsored Research Information Exchange Requirements

IER Number	Exchange Action	Exchange Content	Initiating System	Responding System(s)	Exchange Attribute
IS158-IER1	Send/Receive	Clinical Research Workflow	EHR	EDC	Site identifier, subject identifier, visit identifier, study identifier
IS158-IER2	Send/Receive	Clinical Research Workflow	EDC	EHR	Pseudonymous subject identifier
IS158-IER3	Send	Clinical Research Document	EHR	EDC	Site identifier, subject identifier, visit identifier, study identifier, redacted clinical research document



IER Number	Exchange Action	Exchange Content	Initiating System	Responding System(s)	Exchange Attribute
IS158-IER4	Response	Clinical Research Document	EDC	EHR	CRF pre-populated with appropriate CRD data
IS158-IER5	Send/Receive	Clinical Research Document	EHR	EDC	Includes data not provided by EHR but filled in by site personnel
IS158-IER11	Send/Receive	Clinical Research Document	EHR	Source Archive	Location determined by study site
IS158-IER12	Send/Receive	Laboratory Result Document	Central Lab Facility	EDC	
IS158-IER13	Send/Receive	Imaging Results	Central Radiology Facility	EDC	

2.3 REGISTRY REPORTING SCENARIO

Registry Reporting differs from the Protocol-driven Sponsored Research scenario in the regulatory environment and the requirements of confidentiality. Although registries are not part of the drug approval process, FDA does exercise regulatory oversight, and the requirements for source record archiving do apply. But in some cases, patient participation in a registry is entirely identified, eliminating the need for pseudonyms.

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 patient advocacy organization, disease registry, or government agency. 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.

2.3.1 INFORMATION EXCHANGE REQUIREMENTS FOR REGISTRY REPORTING SCENARIO

Table 2-5 Registry Reporting Information Exchange Requirements summarizes the relationship between the Exchange Action, Exchange Content, and the Initiating and Responding Systems along with Exchange Attributes.

Table 2-5 Registry Reporting Information Exchange Requirements

Information Exchange Requirement Number	Exchange Action	Exchange Content	Initiating System	Responding System(s)	Exchange Attribute
IS158-IER6	Send/Receive	Clinical Research Workflow	EHR	Registry System	Patient identifiers
IS158-IER7	Send/Receive	Clinical Research Workflow	Registry System	EHR	Subject identifier
IS158-IER8	Send	Clinical Research Document, Clinical Research Workflow	EHR	Registry System	Patient ID + C32 complete
IS158-IER9	Response	Clinical Research Workflow	Registry System	EHR	Case report form pre-populated by CRD



IS158-IER10	Send/Receive	Clinical Research Workflow	EHR	Registry System	Includes data not provided by EHR but filled in by site personnel
IS158-IER11	Send/Receive	Clinical Research Workflow	EHR	Source Archive	Location determined by study site

2.4 RESEARCH NETWORK SCENARIO

The research network scenario positions a data aggregator, the research network system, between the participating healthcare sites and the research system, the EDC. This aggregator operates as a mega-site, and the relationship between the research network and the sponsor's system, the EDC, resembles the relationship of one site's EHR to the EDC. Research networks are a recent phenomenon, and configurations vary. This scenario represents one possible implementation of this evolving concept.

Network. Data from a particular study 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 Access Control. 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.

2.4.1 INFORMATION EXCHANGE REQUIREMENTS FOR RESEARCH NETWORK SCENARIO

Table 2-5 Research Network Information Exchange Requirements summarizes the relationship between the Exchange Action, Exchange Content, and the Initiating and Responding Systems along with Exchange Attributes.

Table 2-6 Research Network Information Exchange Requirements

Information Exchange Requirement Number	Exchange Action	Exchange Content	Initiating System	Responding System(s)	Exchange Attribute
IS158-IER1	Request	Clinical Research Workflow	Research network system	EDC	Some data elements may be redacted based on policy configuration
IS158-IER2	Respond	Clinical Research Document	EDC	Research network system	Pseudonymous subject identifier
IS158-IER3	Send/Receive	Clinical Research Document	Research network system	EDC	Site identifier, subject identifier, visit identifier, study identifier, redacted clinical care document
IS158-IER4	Send/Receive	Clinical Research Workflow	EDC	Research network system	Case report form pre-populated with CRD
IS158-IER5	Send/Receive	Clinical Research Document	Research network system	EDC	Includes data not provided by EHR but filled in by site personnel as electronic source document.
IS158-IER11	Send/Receive	Clinical Research Workflow	Research network system	Source Archive	Location determined by study site or research network
IS158-IER12	Send/Receive	Lab Result Document	Central Lab Facility	EDC	
IS158-IER13	Send/Receive	Imaging Results	Central Radiology Facility	EDC	



2.5 SYSTEM DESCRIPTION

The following table lists systems involved in the above listed scenarios, and identifies the stakeholders served by those involved systems.

Table 2-7 System Names and Descriptions

System Name	System Description	Stakeholders
Electronic Health Record (EHR) System	The Electronic Health Record (EHR) System is a secure, real-time, point-of-care, patient-centric information resource for clinicians located at the healthcare site	Healthcare Delivery Organizations, Ancillary Entities, Clinicians, Care Delivery Actor
Electronic Data Capture (EDC) System	Referred to as 'Site Study Data System' in Use Case Table 7.1. This system may handle data validation or it may be handled in a separate application. The EDC system is managed by the sponsor or its agents	Sponsor, Clinical Research Organization (CRO)
Clinical Research Repository (Clinical Data Management System (CDMS))	Repository where data are streamed for housing and cleansing. Out of scope; included for context only	Sponsor, Clinical Research Organization (CRO)
Protocol Development System	System used to author protocols. Out of scope; included for context only	Sponsor
Electronic Source Document Archive	A system that embodies RFD Form Archiver interface, and stores electronic source information on behalf of the site. Can be an add-on to the EHR, a standalone application at the site, or an application hosted by a trusted third party to the site	Site, that is any healthcare site that is participating in a clinical research study
Safety Monitoring System	System to which adverse events are reported. Out of scope; included for context only	Site
Institutional Review Board (IRB) System	Committee whose primary responsibility is to protect the rights and welfare of human research subjects through appropriate review and approvals prior to beginning research. Out of scope; included for context only	Site
Reviewer System	"Individuals or organizations that review the final tabulated dataset once the study is complete"	Reviewer
Registry System	"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." Relevant to scenario 2 only	Sponsor, Clinical Research Organization (CRO)
Distributed Clinical Research Network System	An "intermediate database or data repository" that serves a network of healthcare and research sites. Relevant to scenario 3 only	Site
Central Diagnostic System	"A central laboratory or imaging diagnostic center" to which research specific lab and image work is referred	Labs, Sponsor
Analysis and Reporting System	Sponsor-based system. Performs analysis on study data	Sponsor



3.0 DESIGN SPECIFICATION

Section 3.0 identifies the Capabilities used to meet the requirements identified in Section 2.0 Requirements and describes how to orchestrate this set of Capabilities to meet those requirements. The following table details how this section of the document is targeted to specific readers. Each of the stakeholders listed in this table are more fully defined in a separate appendix. This table is provided as an aid to readers to assist with identifying specific areas of focus. Readers are encouraged to review all sections of this document to further their understanding of HITSP's work.

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Document Section	Section Number	Intended Audience	Information Contained
Section 3.0 Design Specification	3.1 Capabilities Used	Architects Business Analysts Development Team	For each Information Exchange Requirement (IER) identified in Section 2.0, a corresponding Capability is associated and mapped. A reader can review how specific Capabilities meet information exchange needs. A diagram is also provided to show the interchange of data among systems identified in this Interoperability Specification
	3.2 Capability Orchestration	Architects Development Team	The core of the design in the Interoperability Specification is documented here. This solution shows orchestration of Capabilities to meet the specific Information Exchange Requirements (IER) in Section 3.1 The design also identifies conditions and constraints, as well as any content subsets specific to the solution

3.1 CAPABILITIES USED

The table below lists the Capabilities used in this Interoperability Specification, and relates them to the information exchange requirements from Table 2-2 that the Capability satisfies. The information exchanges listed are the relevant information exchanges from the underlying Capability.

Table 3-2 Capabilities Used

Capability	Capability Summary	Capability IE Used	IERs Satisfied
HITSP/CAP127 – Communicate Lab Results Document	This Capability addresses interoperability requirements that support the communication of a set of structured laboratory results related to a patient in a context set by the source of the document who is attesting to its content. Non-ordering Providers of Care access historical laboratory results as documents and "copy-to" Providers of Care may receive document availability notifications to retrieve such lab report documents. Lab Report content creators shall support HITSP specified coded terminologies as defined by specific content subsets specified in this Capability for: General Laboratory Test Results; Microbiology Test Results This Capability may use content anonymization	A – Send/Receive Lab Report Document	IS158-IER12
HITSP/CAP128 – Communicate Imaging Information	This Capability addresses interoperability requirements that support the communication of a set of imaging results (i.e., reports, image series from imaging studies) related to a patient in a context set. This is done by an Imaging System acting as the information source attesting to its content. This Capability may use content anonymization	A – Send/Receive Imaging Results	IS158-IER13
HITSP/CAP135 – Retrieve and Populate Form	This Capability addresses interoperability requirements to support the upload of specific	A – Send Pre-population Data	IS158-IER3 IS158-IER8

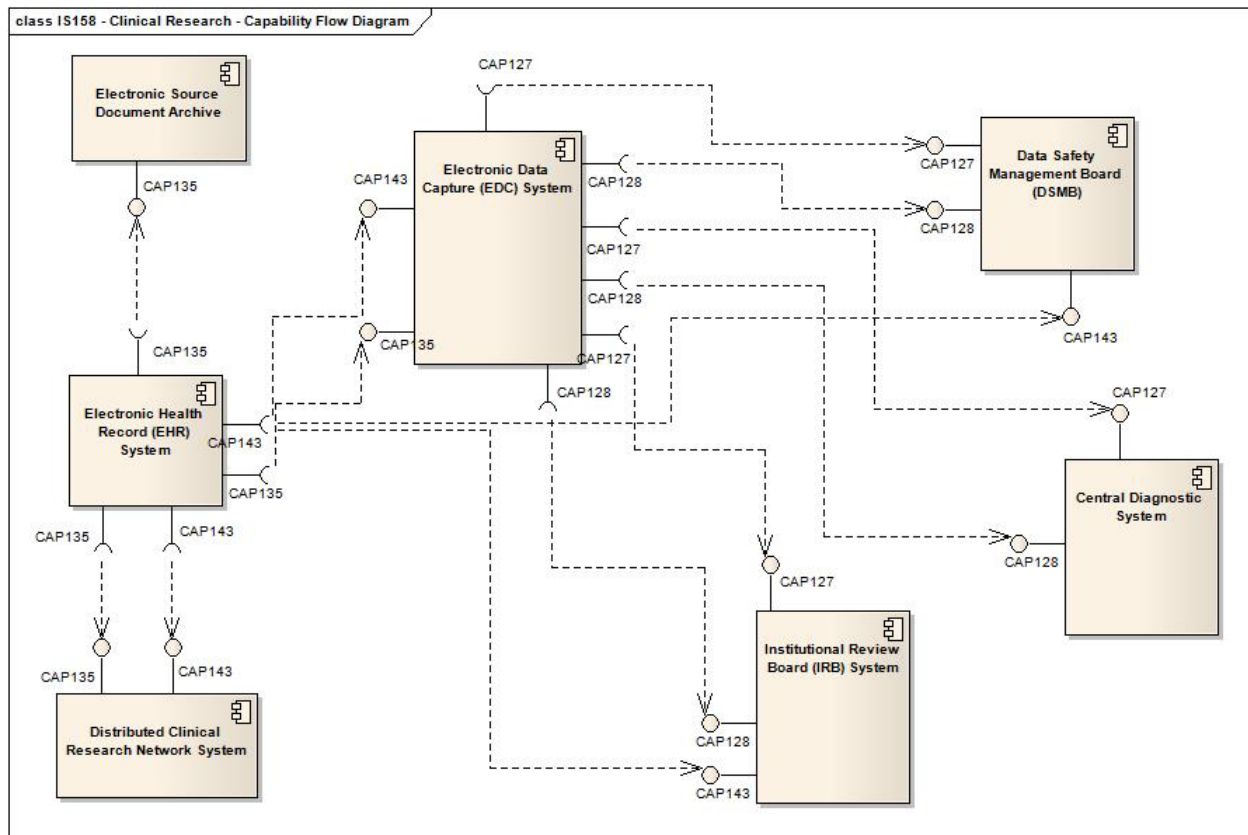


Capability	Capability Summary	Capability IE Used	IEs Satisfied
	<p>captured data (e.g. public health surveillance reportable conditions, healthcare associated infection reporting) to Public Health Monitoring Systems and Quality Organizations Systems and Clinical Research Systems. The forms presented may be pre-populated by information provided by the clinical or laboratory information systems to avoid manual re-entry. A number of supplemental information variables may be captured from within the user's clinical information system to improve the workflow and timeliness of required reporting. One or more types of form content may be supported:</p> <p>Pre-population for Public Health Case Reports from Structured Documents using CDA</p> <p>Pre-population for Quality Data from Structured Documents using CDA</p> <p>Pre-population of Clinical Research Reports from structured documents</p> <p>No pre-population content</p> <p>Systems may optionally support the means to retrieve request for clarifications</p>	<p>B - Receive Pre-population Data</p> <p>C - Send Pre-populated Form</p> <p>D - Receive Pre-populated Form</p> <p>E - Send Data Instance</p> <p>F - Receive Data Instance</p>	<p>IS158-IER9</p> <p>IS158-IER11</p>
HITSP/CAP143 – Manage Consumer Preference and Consents	<p>This Capability addresses management of consumer preferences and consents as an acknowledgement of a privacy policy. This Capability is used to capture a patient or consumer agreement to one or more privacy policies; where examples of a privacy policy may represent a consent, dissent, authorization for data use, authorization for organizational access, or authorization for a specific clinical trial. This Capability also supports the recording of changes to prior privacy policies such as when a patient changes their mind on participation or requests that data no-longer be made available because they have left the region</p>	<p>B – Request & Response Consent Directives</p>	<p>IS158-IER1</p> <p>IS158-IER2</p> <p>IS158-IER3</p> <p>IS158-IER4</p> <p>IS158-IER5</p> <p>IS158-IER6</p> <p>IS158-IER7</p> <p>IS158-IER8</p> <p>IS158-IER9</p> <p>IS158-IER10</p>

The following diagram shows how systems use Capabilities to complete the full Interoperability Specification. The diagram is purposely created to be architecturally neutral. In some settings a given system role within a Capability will be filled by more than one system in the Interoperability Specification. In many settings, one system may implement multiple Capabilities as shown in the diagram. There are many potential combinations of systems using these Capabilities in different architectures as discussed in Section 3.2.2 Implementation Variants. The diagram therefore uses one example that includes all systems.



Figure 3-1 Diagram Showing Capabilities Used Between Systems



3.2 CAPABILITY ORCHESTRATION

This section describes how the Capabilities identified above are orchestrated to achieve the aims of the Harmonization Request (such as a Use Case) addressed by this Interoperability Specification. The orchestration identifies systems that fill the system roles in the Capabilities to achieve the desired data flows.

Table 3-3 Orchestration of Capabilities by System

System	Capability	System Role	System Role Option	Condition
Electronic Health Record (EHR) System	HITSP/CAP135 – Retrieve and Populate Form	Form Filler	R	
	HITSP/CAP143 – Manage Consumer Preference and Consents	Consent Creator	R	
Electronic Data Capture System	HITSP/CAP127 – Communicate Lab Results Document	Document Consumer	O	
	HITSP/CAP128 – Communicate Imaging Information	Imaging Document Consumer	O	
	HITSP/CAP135 – Retrieve and Populate Form	Form Manager	R	
	HITSP/CAP143 – Manage Consumer Preference and Consents	Consent Consumer	R	



System	Capability	System Role	System Role Option	Condition
Clinical Research Repository, also called Clinical Data Management System (CDMS)			Out of scope	
Protocol Development System			Out of scope	
Electronic Source Document Archive	HITSP/CAP135 – Retrieve and Populate Form	Form Archiver	O	C[101]
Data Safety Management Board (DSMB)	HITSP/CAP127 – Communicate Lab Results Document	Content Consumer	R	
	HITSP/CAP128 – Communicate Imaging Information	Imaging Document Consumer	R	
	HITSP/CAP143 – Manage Consumer Preference and Consents	Consent Consumer	R	
Institutional Review Board (IRB) system	HITSP/CAP127 – Communicate Lab Results Document	Content Consumer	R	
	HITSP/CAP128 – Communicate Imaging Information	Imaging Document Consumer	R	
	HITSP/CAP143 – Manage Consumer Preference and Consents	Consent Consumer	R	
Distributed Clinical Research Network System	HITSP/CAP135 – Retrieve and Populate Form	Form Filler	R	
	HITSP/CAP143 – Manage Consumer Preference and Consents	Consent Creator	R	
Central Diagnostic system	HITSP/CAP127 – Communicate Lab Results Document	Content Creator	R	
	HITSP/CAP128 – Communicate Imaging Information	Send Document	R	
Analysis and Reporting System			Out of scope	

Table 3-3 lists the orchestration of Capabilities by system to meet the information exchange requirements described in Section 2.0. Subsets of these systems perform information exchanges according to one or more of the Capabilities identified in this specification. The Capabilities are annotated on the diagrams. The in-scope requirements are supported by Capabilities either previously specified by HITSP or new Capabilities introduced in this section. Optionality is expressed as Required (R), Optional (O) or Conditional (C). If the optionality is Conditional, the applicable conditions are given in Table 3-4 below.

Table 3-3 Orchestration of Capabilities by System

System	Capability	System Role	System Role Option	Condition
Electronic Health Record (EHR) System	HITSP/CAP135 – Retrieve and Populate Form	Form Filler	R	
	HITSP/CAP143 – Manage Consumer Preference and Consents	Consent Creator	R	
Electronic Data Capture System	HITSP/CAP127 – Communicate Lab Results Document	Document Consumer	O	
	HITSP/CAP128 – Communicate Imaging Information	Imaging Document Consumer	O	



System	Capability	System Role	System Role Option	Condition
	HITSP/CAP135 – Retrieve and Populate Form	Form Manager	R	
	HITSP/CAP143 – Manage Consumer Preference and Consents	Consent Consumer	R	
Clinical Research Repository, also called Clinical Data Management System (CDMS)			Out of scope	
Protocol Development System			Out of scope	
Electronic Source Document Archive	HITSP/CAP135 – Retrieve and Populate Form	Form Archiver	O	C[101]
Data Safety Management Board (DSMB)	HITSP/CAP127 – Communicate Lab Results Document	Content Consumer	R	
	HITSP/CAP128 – Communicate Imaging Information	Imaging Document Consumer	R	
	HITSP/CAP143 – Manage Consumer Preference and Consents	Consent Consumer	R	
Institutional Review Board (IRB) system	HITSP/CAP127 – Communicate Lab Results Document	Content Consumer	R	
	HITSP/CAP128 – Communicate Imaging Information	Imaging Document Consumer	R	
	HITSP/CAP143 – Manage Consumer Preference and Consents	Consent Consumer	R	
Distributed Clinical Research Network System	HITSP/CAP135 – Retrieve and Populate Form	Form Filler	R	
	HITSP/CAP143 – Manage Consumer Preference and Consents	Consent Creator	R	
Central Diagnostic system	HITSP/CAP127 – Communicate Lab Results Document	Content Creator	R	
	HITSP/CAP128 – Communicate Imaging Information	Send Document	R	
Analysis and Reporting System			Out of scope	

Optionality Legend: “R” for Required, “O” for Optional, or “C” for Conditional

Table 3-4 below lists the conditions applicable to the orchestration (see above table) of the Capabilities engaged in this Interoperability Specification.

Table 3-4 Conditions

Condition Code	Condition Description
IS158[101]	Optional for scenario 2; required for scenarios 1 and 3

3.2.1 CONTENT SUBSETS

Content subsets are appropriate subsets of the data content supported by the Capability that may be sent by the system and/or received in a specific information exchange. There may be no relevant subsets identified.



Not applicable for this Interoperability Specification.

3.2.2 IMPLEMENTATION VARIANTS

This specification is intended to support multiple implementation architectures. Described below are likely scenarios, all leveraging one or more of the Information Exchange Requirements identified in Table 2-6. In some environments, information may be analyzed and aggregated locally and in others, the service may be provided by a trusted third party. The following list of example environments is not an exhaustive list:

Table 3-5 Implementation Variant 1

Variant 1: Archive
The Forms Archiver can be implemented either as a local service hosted at the patient care site or through a trusted third party

Table 3-6 lists a number of general constraints applicable to this specification. They include assumptions, a number of pre-conditions and post-conditions as well as external trigger events that play a critical role in implementing this specification.

Table 3-6 Orchestration Constraints

Constraint ID	Constraint	Type of Constraint
IS158[CT1-01]	All applicable HITSP Security and Privacy constructs are implemented as required.	Pre-condition
IS158[CT1-02]	Policies for sharing data are defined in agreements	Pre-condition
IS158[CT1-03]	Patient consents are in place.	Pre-condition

3.2.3 CONSTRAINTS ON REQUIRED CAPABILITIES

This section describes the constraints that further limit the Capabilities that are used by this Interoperability Specification.

Table 3-7 Additional Constraints on Required Capabilities

Constraint ID	Data Element	Capability	Constraint	Constraint Type	Purpose (Reason for this constraint)
IS158[DE1-01]	Data sent to the EDC, IRB, and DSMB must be pseudonymized or anonymized unless otherwise permitted through legal and out-of-band arrangements	HITSP/CAP135 – Retrieve and Populate Form	Information Content	Pre-condition	Required to protect the confidentiality of the study participant whose personal health information is sent for analysis
IS158[DE1-02]	Data sent to the EDC, IRB, or DSMB must be redacted to match the requirements of the research protocol	HITSP/CAP135 – Retrieve and Populate Form	Information Content	Pre-condition	Required to comply with regulations limiting the confidentiality of subjects in clinical studies



4.0 CAPABILITY GAPS

Section 4.0 identifies gaps not met by existing Capabilities but needed to achieve the aims of the Harmonization Request for which this Interoperability Specification is written. This includes overlaps in Capabilities as well. The following table details how this section of the document is targeted to specific readers. Each of the stakeholders listed in this table are more fully defined in a separate appendix. This table is provided as an aid to readers to assist with identifying specific areas of focus. Readers are encouraged to review all sections of this document to further their understanding of HITSP's work.

Table 4-1 Reader's Guide for Section 4.0

Document Section	Section Number	Intended Audience	Information Contained
Section 4.0	4.0 Capability Gaps	Business Analysts Development Team Architects	Gaps specific to Capabilities used as part of this Interoperability Specification are reviewed in this section to determine why specific information exchange requirements may not yet be met or defined. Readers should check this section to track the progress of gap resolution

The following table identifies gaps not met by or overlapping with existing Capabilities as described above.

Table 4-2 Capability Gaps

IER Gap Description	Responsible HITSP TC	Design Approach	Required Standards Now Unavailable for Constructs	SDO Working on Unavailable Standards	Expected Availability
IS158-IER3	Population Perspective	Modify Capability 135, plus create new construct for redaction.	Redaction Services. The data sent from the EHR to the EDC must conform to the protocol. Currently there is a gap in the ability to redact the CCD to conform to the protocol-required data as specified in the case report form	IHE	June 2010. A new IHE profile called Redaction Services has been accepted for inclusion in the Quality, Research, and Public Health (QRPH) domain



5.0 APPENDIX

The following sections include relevant materials referenced throughout this document. The following table details how this section of the document is targeted to specific readers. Each of the stakeholders listed in this table are more fully defined in a separate appendix. This table is provided as an aid to readers to assist them in identifying sections to focus on. Readers are encouraged to review all sections of this document to further their understanding of HITSP's work.

Table 5-1 Reader's Guide for Section 5.0

Document Section	Section Number	Intended Audience	Information Contained
Section 5.0	5.1 Provisional Exchange Content Description	Architects	Supporting information is provided for HITSP exchange content that is identified as provisional (due to gaps identified in the previous section)
	5.2 Provisional Data Requirements	Architects	Supporting information is provided for HITSP data requirements that are associated with provisional exchange content identified in Section 5.1
	5.3 Harmonization Request Traceability	Architects Business Analysts	A complete mapping of HITSP information exchange requirements to functional requirements is provided in this section. Readers can trace IER's to underlying Use Case events and actions (in those instances where a Use Case exists) or to functional requirements defined as part of an official standards Harmonization Request

5.1 EXCHANGE CONTENT DESCRIPTIONS

The exchange content descriptions answer one or more data requirements, and map to existing or planned HITSP constructs. In this section, exchange content descriptions identified for IERs that address gaps are described.

Table 5-2 New Exchange Content Data Requirements

Exchange Content Identifier	Exchange Content Name	Exchange Content Definition	Data Requirements
EC1	C151	Clinical Research Document (CRD) redacted to match the requirements of the protocol	DR4 DR5 DR6 DR7 DR8 DR9 DR10 DR12 DR14
EC2	C151	CRD expanded to include protocol and visit specific data not covered in the pre-population	DR4 DR5 DR6 DR7 DR8 DR9 DR10 DR12 DR13 DR14



Exchange Content Identifier	Exchange Content Name	Exchange Content Definition	Data Requirements
EC3	C156	Identifiers for patient, study, site, investigator	DR1 DR2 DR3 DR14
EC4	C76	Adverse Event report	DR12
EC5	C37	HITSP Lab Report Document Component	DR11
EC6	TP89	HITSP Sharing Imaging Results Transaction Package	DR11

5.2 DATA REQUIREMENTS

In this section, data requirement descriptions identified for exchange contents listed above are described.

Table 5-3 Data Requirements

Data Requirement Number (DR)	Description	Data
DR1	Planning and Reporting Requirements (Sources: CDISC Protocol Representation, CDISC Trial Design Model, HL7 Study Design)	Informed consents Eligibility verification Study design template
DR2	Study Identifiers (data elements taken from CDISC Protocol Representation and HL7 Study Design)	Study identifier - Unique Identifier for a study within a submission Study Site identifier - The unique identification assigned to a study site by a study sponsor StudyInvestigator.identifier The unique identification given to a study investigator by a study sponsor StudyInvestigator.dateRange The date and time on which an investigator's participation in a specific study begins and ends StudyInvestigator.signatureText The signed name of the investigator who is responsible for completing a form or report for a clinical trial. Investigator Name A non-unique textual identifier or moniker of a person. For example, proper names, nicknames, legal names of persons, etc. Study visit Study encounter - any participation by a participant



Data Requirement Number (DR)	Description	Data
DR3	Subject Demographics (C83 Section 2.2.2.1, 2.2.2.2, 2.2.2.7)(HL7 Subject Data)	Subject ID Person ID Date of birth Gender Race (code list to be determined) Ethnic/cultural background Native language Address Phone Patient Name Marital status Religious affiliation Multiple birth indicator Death indicator Deceased date/time Birth place Date and time collected NOTE: Protected Health Information (Individually Identifiable Health Information) can be used or not according to the privacy rules in play. Note that Scenario 2, registry reporting, can be fully identified whereas scenario 1 is typically pseudonymized
DR4	Prior and Concomitant Medications (C83 Section 2.2.2.8)	Medication Indication Dose Timing of medication Frequency Route Rate Length of time on medication Date and time collected
DR5	Medical History (C83 Section 2.2.2.7)	Type of history Allergies Surgeries Family history Diet Exercise Concomitant therapies Date and time collected
DR6	Physical Examination (C83 Section 2.2.2.7)	Body system examined Results Clinical comments Date and time collected
DR7	Substance Use (C83 Section 2.2.2.8)	Type of substance Occurrence of use Frequency and duration Date and time collected
DR8	Vital Signs: (C83 Section 2.2.2.14)	Result identifier Result date/time Result type Result status Result value Result interpretation Result reference range



Data Requirement Number (DR)	Description	Data
DR9	Family History (C83 Section 2.2.2.18)	Pedigree Family member information Family member demographics Family member relationship free text Family member name Family member date of birth Family member race Family member ethnicity Family member relationship Family member medical history Family member medical history Family member condition Family member age Family member cause of death Family member age at death Family member biological sex Family member multiple birth status Family member age Family member genetic test code Family member genetic test name Family member genetic test result Family member genetic test date
DR10	List of Surgeries (C83 Section 2.2.2.17)	Procedures Procedure identifier Procedure type Procedure free text type Procedure date/time Procedure provider
DR11	Diagnostic Data (C83 Section 2.2.2.15)	Result event entry Result identifier Result date/time Result type Result status Result value Result interpretation Result reference range
DR12	Adverse Clinical Events (C83 Section 2.2.2.6)	Description of event Seriousness Severity Action taken Outcome Date and time collected
DR13	Protocol-specific data not included in Clinical Research Document	Study specific data
DR14	Informed consent	Date and time consent form was executed

5.3 HARMONIZATION REQUEST TRACEABILITY

This section describes the traceability to the Harmonization Request for which this IS is written. The Traceability may be described in terms of events and actions, or in terms of functional requirements.



Table 5-4 Mapping of Use Case Actions to Information Exchange Requirements

Event	Action	IER	Initiating System	Responding System	Data Requirements	Comments
7.1.1 Event: Complete and communicate study design	7.1.1.1 Action: Develop study design and protocol	N/A	Protocol Development System	N/A	DR1	Out of scope. Action Included in scenario for context only
	7.1.1.2 Action: Working with the Principal Investigator	N/A	Protocol Development System	EHR	DR1	Out of scope. Action Included in scenario for context only
	7.1.1.3 Action: Sponsor sends design and protocol to investigative site and Reviewer(s)	N/A	Protocol Development System	Reviewer's system, CRO, EDC, EHR	DR1	Out of scope. Action Included in scenario for context only
7.1.2 Event: Send case reporting form (CRF Template) from centrally hosted server	7.1.2.1 Action: Sponsor sends CRF to the Investigative Site data manager	N/A	Protocol Development System	EDC, EHR	DR1	Out of scope. Action Included in scenario for context only
7.1.3 Event: Receive, validate and tabulate CRF study data	7.1.3.1 Action: Study data are received from the Investigative Site	N/A	EHR	EDC	DR2 – DR9	Out of scope. Action Included in scenario for context only
	7.1.3.2 Action: Study data are validated	N/A	Clinical Research Repository (Clinical Data Management System (CDMS))	N/A	DR2 – DR9	Out of scope. Action is internal to one system
	7.1.3.3 Action: Study data are tabulated	N/A	Research Repository	N/A	DR2 – DR9	Out of scope. Action is internal to one system
7.1.4 Event: Monitor site as necessary	7.1.4.1 Action: Sponsor monitors investigative site	N/A	Research Repository, EDC	EHR	DR2 – DR9	Out of scope. Beyond boundaries of data exchange
7.1.5 Event: Transmit interim data	7.1.5.1 Action: Interim data are transmitted to a Reviewer	N/A	Research Repository	Reviewer	DR2 – DR9	Out of scope. Beyond boundaries of data exchange
7.1.6 Event: Transmit final data	7.1.6.1 Action: Final data and application for approval is sent to the Reviewer	N/A	Research Repository, Analysis and Reporting System	Reviewer	DR1 – DR9	Out of scope. Beyond boundaries of data exchange
7.2.1 Event: Receive study design including CRF parameters into EHR system	7.2.1.1 Action: Site receives study design	N/A	EDC	EHR	DR1	Out of scope. Action Included in scenario for context only
	7.2.1.2 Action: Study sent to Institutional Review Board (IRB) for approval	N/A	EDC	IRB	DR1	Out of scope. Action Included in scenario for context only
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	N/A	EHR	N/A	Application specific	Out of scope. Action is internal to one system



Event	Action	IER	Initiating System	Responding System	Data Requirements	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	IER1	EHR	EDC	DR1 - 3	In scope. EHR identifies patient as a candidate subject for the study and requests subject identifier from the study data system (EDC). Patient may receive a temporary screening number before the permanent enrollment number is assigned. Certificate of Confidentiality may prevent EHR from identifying a patient as an enrolled subject or it may limit such identification to certain 'need to know' EHR users
7.2.4 Event: Perform clinical activities	7.2.4.1 Action: Perform all patient activities related to the clinical study	N/A	EHR	N/A		Out of scope. Action is internal to one system
	7.2.4.2 Action: Record all study related information to form the source document.	N/A	EHR	N/A	DR2 – DR9	Out of scope. Action is internal to one system
7.2.5 Event: Send information to study data system	7.2.5.1 Action: Source document is sent to the study data system	IER3, IER5	EHR	EDC	DR2 – DR9	In scope. Must ensure that only protocol-specified data are sent from the EHR. This action takes place in two parts: 1. Send EHR extract and request form; 2. Send completed CRF. IER3 and IER5
7.2.6 Event: Extract core dataset from EHR and send information to registry or database	7.2.6.1 Action: Information is sent to registries or other databases. (Scenario 2 only)	IER8, IER10	EHR	Registry system	DR2 – DR9	In scope, Scenario 2. This action takes place in two parts: 1. Send DHR extract and request form; 2. Send complete CRF return. IER8 and IER10
7.2.7 Event: Periodically exchange data from EHR in a distributed network	7.2.7.1 Action: Data are exchanged with the clinical system (EHR) and sent to an intermediate database	IER3	EHR	Distributed Clinical Research Network system	DR2 – DR9	In scope for Scenario 3
7.3.1 Event: Enroll subject in study	7.3.1.1 Action: Patient is enrolled in study	IER2	EDC	EHR	DR2	In scope. Subject identifier is returned to EHR ('Enrolled' means to be randomized into trial) IER2



Event	Action	IER	Initiating System	Responding System	Data Requirements	Comments
	7.3.1.2 Alternative Action	N/A	EDC	N/A	N/A	Out of scope. Null case where patient does not meet criteria. Sponsor may still have interest in the subject information
7.3.2 Event: Retrieve case reporting form (CRF Template)	7.3.2.1 Action: Site data manager obtains a CRF template from a server managed by the study sponsor	N/A	Protocol Development System	EDC, EHR	DR1	Out of scope. Action included in scenario for context only
7.3.3 Event: Receive data from clinical personnel or EHR	7.3.3.1 Action: Data Manager receives the data from the clinical study coordinator and enters the data into a study database	N/A		EDC	DR2 – DR9	Out of scope. Action included in scenario for context only
	7.3.3.2 Alternative Action: Data from the EHR is pre-populated on an electronic form with study specific information entered electronically	IER4, IER5, IER9, IER10	EDC	EHR	DR2 – DR9	In scope. Action takes place two steps: 1. Pre-population data received and mapped to form and returned to EHR (IER4, IER9); 2. Final completed data form received from EHR (IER5, IER10)
7.3.4 Event: Receive and incorporate results from Central Diagnostics into study database	7.3.4.1 Action: Diagnostic information is received and incorporated into the study database	IER12, IER13	Central Diagnostic System	EDC or EHR	DR11	In scope. IER12, IER13
7.3.5 Event: Complete, validate and transmit CRF to Sponsor and e-Source Document Archive	7.3.5.1 Action: Data are completed and validated	N/A	EDC	EHR, Source archive	DR2 – DR9	Out of scope. Action Included in scenario for context only
	7.3.5.2 Action: Various safety boards' monitor the study	N/A	EDC, Research Repository	DSMB, IRB	DR2 – DR9	Out of scope. Action Included in scenario for context only
	7.3.5.3 Action: CRF Data are transmitted to sponsor	N/A	EDC	Research Repository	DR2 – DR9	Out of scope. Action Included in scenario for context only
	7.3.5.3a Alternative Action: Additional clarification of transmitted CRF data	N/A	EDC, EHR	Research Repository		Out of scope. Action Included in scenario for context only
	7.3.5.4 Action: CRF Data are transmitted to Electronic Source Document Archive	IER11	EHR	Source Archive	DR2 – DR9	In scope. Data are archived at the same time that data are received at the EDC system



Event	Action	IER	Initiating System	Responding System	Data Requirements	Comments
7.3.6 Event: Exchange aggregated longitudinal data from distributed network with organizational database	7.3.6.1 Action: Longitudinal information is aggregated and sent to an organizational database	IER3	EHR	Distributed Clinical Research Network System	DR2 – DR9	Scenario 3. IER3
7.4.1 Event: Receive study design including CRF parameters	7.4.1.1 Action: Reviewer receives a version of the study design and CRF parameters	N/A	Protocol Development System	Reviewer System	DR1	Out of scope. Action Included in scenario for context only
7.4.2 Event: Register study	7.4.2.1 Action: Clinical study is registered with the reviewer	N/A	Protocol Development System	Reviewer System	DR1	Out of scope. Action Included in scenario for context only
7.4.3 Event: Receive interim data and/or audits	7.4.3.1 Action: Sponsor sends interim data reports and/or audits to the reviewer	N/A	Research Repository	Reviewer System	DR2 – DR9	Out of scope. Action Included in scenario for context only
	7.4.3.2 Action: Sponsor and reviewer may exchange information regarding the ongoing study	N/A	Research Repository, Reviewer System	Reviewer system, Research Repository	DR2 – DR9	Out of scope. Action Included in scenario for context only
7.4.4 Event: Receive final data	7.4.4.1 Action: Sponsor sends final data at the end of the clinical study	N/A	Research Repository	Reviewer System	DR2 – DR9	Out of scope. Action Included in scenario for context only
7.5.1 Event: Receive aggregated data from distributed network	7.5.1.1 Action: Aggregated Data are received by the organizational database	N/A	Research Repository	Distributed Clinical Research Network System	DR2 – DR9	Out of scope. Action Included in scenario for context only



6.0 DOCUMENT UPDATES

The following sections provide the details of updates made to this document.

6.1 NOVEMBER 9, 2009

No changes. This is the first published version of the document.

6.2 JANUARY 18, 2010

- Migrated to the new HITSP Interoperability Specification template Version 2.0
- Updated Section 1.1, Interoperability Specification Overview to add clarity
- Modified Section 2.2, Protocol-Driven Sponsored Research Scenario to add clarity
- Updated Section 2.3, Registry Reporting Scenario to add clarity
- Updated Table 3-3, Orchestration of Capabilities by System
- Added Table 4-2 Capability Gaps
- Updated HITSP/C83 Content Module references in Table 5-2 New Exchange Content Data Requirements New Exchange Content Data Requirements

The associated comment numbers for these updates are as follows:

8556, 8559, 8561, 8562, 8614, 8631, 8635, 8680, 8731, 8732, 8764, 8766, 8793, 9063, 9370, 9374, 9376, and 9731

The full text of the comments along with the Technical Committee's disposition can be reviewed on the [HITSP Public Web Site](#).

6.3 JANUARY 25, 2010

Upon approval by the HITSP Panel on January 25, 2010, this document is now Released for Implementation.

