Electronic Health Records/Clinical Research

EHR/CR
User Requirements Document

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EHR/CR Functional Profile Working Group
eClinical Forum,
PhRMA EDC/eSource Task Force

Co-Chairs

John D. Mestler
Suzanne Bishop
Richard Perkins
Catherine Celingant

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This User Requirements document is the first deliverable for the Electronic Health Records/ Clinical Research (EHR/CR) Working Group. It identifies, at a high level, user requirements necessary for using electronic records from healthcare systems for regulated clinical research[1]. This document, in its draft version, was intended as a tool to foster discussion among stakeholders. Stakeholder comments have been received, reviewed, and incorporated within this document to enhance the original release. This user requirements document has been used as a basis for qualifying clinical research criteria for the HL7 EHR Functional Model and the EuroRec EHR Repository which will be provided by future deliverables in each of the HL7 and EuroRec formats.

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[1] Throughout this document, 'clinical research' is used to imply regulated clinical research.

1. This Document

This User Requirements document will clarify the minimum requirements to use healthcare systems as the data source for clinical research today, in order to ensure the reliability of clinical research data from EHR (Electronic Health Record) systems. This is a first deliverable and is intended to generate discussion within the Healthcare and Clinical Research communities. Further to this document, user requirements will be mapped to HL7 and EuroRec functional models in separate deliverables, and will be submitted to these organizations in their respective formats. This document will also be used to investigate ways that research requirements might be incorporated into the CCHIT (Certification Commission for Health Information Technology) certification process. (HL7, or Health Level 7, is a standards development organization (SDO) working in the healthcare arena, EuroRec (European Quality Labeling and Certification of Electronic Health Record) is the European Union EHR certification committee, under the direction of European Institute for Health Records (EuroRec), and CCHIT is the US Certification Commission for Health Information Technology.) As this document will be used as the basis to produce two similar EHR/CR Functional Profiles; one in the HL7 format and one in the EuroRec format, we expect both of these submissions to represent the same user requirements, ensuring global consistency with respect to profile definition. While the intent of this document is to clearly identify the *minimum* requirements for using data from EHR systems for clinical research, it provides the evolutionary vision of technology and processes toward an ultimate goal of healthcare and research being natural partners. A supplement to this user requirements document is provided to discuss how these systems and processes might develop in the future (in an integrated / connected environment) toward the ultimate goal of research being a natural progression of healthcare.

2. The EHR/CR Working Group

The global EHR/CR Functional Profile Project is organized by the eClinical Forum and the PhRMA EDC/eSource Taskforce and is a collaborative effort between the bio-pharmaceutical and healthcare industries and associated vendors and regulators. The goal is to expand and adapt the functionality of EHR and associated systems, networks, and processes to support clinical research. Both the global eClinical Forum and PhRMA are not-for-profit professional associations supporting bio-pharmaceutical research. The work of the EHR/CR Working Group is funded by Gold Level partners, Procter and Gamble, Pfizer, and Eli Lilly, and other pharmaceutical industry contributors (see Appendix 2 for a list of project participants).

3. Feedback

The development of the EHR/CR Functional Profile uses the approaches defined by HL7 and EuroRec. That is to say that everyone's contribution or concern will be taken into consideration. Feedback on this User Requirements document as well as all other deliverables from this Working Group is welcome and encouraged. Please submit comments through our website: www.ehrcr.org.

4. Project Overview

The global EHR/CR Functional Profile Project is a collaborative effort to expand and adapt the functionality of EHR and associated systems, networks, and processes to support clinical research. The project is aimed at developing a Functional Profile that identifies critical capabilities for the conduct of clinical research utilizing EHR systems and establishes conformance to the HL7 EHR Functional Model. and the EuroRec EHR Repository.

The main project objectives are:

- To ensure that EHR systems, when used to collect source data in support of claims made regarding the safety and efficacy of any regulated research, can be trusted by authorities to be a 'reliable'[2] data source.

[2] Reliability in this document is meant to meet the requirements as outlined in the FDA CSUCI Guidance for Industry (May 2007; http://www.fda.gov/cder/guidance/7359fnl.pdf) : There is an increasing use of computerized

- To further expand the use of EHR systems for clinical research processes such that clinical research is optimized for clinics and hospitals, allowing new therapies to be available to patients in the shortest time at the lowest cost.
- To expand access to clinical trials for all patients, including underserved populations, and enhance safety monitoring of the trials.

Achieving these objectives is of critical importance to the future of clinical research:

- The time and costs associated with clinical research by investigators, academia, government agencies, and industry have escalated. This has resulted in fewer new innovative medicines, more expensive and late delivery of therapies, failure to explore niche markets of high medical need, and the tendency to focus research resources on environments offering higher return on investment. Creating an environment for more efficient clinical research will help reduce cost and time and increase productivity.
- Early clarification of the requirements for clinical research (both for clinical study conduct and research uses secondary to this) can facilitate their incorporation into EHR system development work ongoing today, and into plans for future expansion of these systems. Some of these secondary uses require little additional functionality over that already provided with commercial EHR systems and benefits could be realized right away. Some examples of secondary use include clinical study recruitment, drug safety & surveillance, retrospective analyses and prospective studies. (Further examples of secondary use are discussed in the Supplement, section A2.3.)

This is the first step to build upon current models being done by HL7 and EuroRec, and to develop criteria at a global level that can facilitate the conduct of global clinical research.

More information on the purpose, goals, and supporting organizations for this project can be obtained from the project website, www.ehrcr.org, by reviewing the document “EHR/CR Functional Profile, Global Project and Profile Description Document”.

5. Approach

Clinical computing is an evolving field and many of the functions desired of an EHR system may not be available at this time. Certain functions, such as EHR system interoperability across country/state/territory healthcare providers, may not be feasible or essential now. Nevertheless, it is important to outline major trends and articulate a vision for functionality (especially interoperability) for the future. Furthermore, the delineation of desirable functionalities for future implementation and adoption should guide vendors in their development efforts, and help purchasers develop and articulate their strategic vision for future functional requirements.

With this in mind, we have defined the scope of the EHR/CR Functional Profile as *what* is necessary to be able to use data from any EHR system for the purpose of regulated clinical studies. (It is important to note that the scope of the project does not include the definition of *how* the functional requirements could be met.) A majority of this functionality is already identified in the HL7 and EuroRec Functional Models as being critical for healthcare systems as well. Regulatory needs for clinical research that do not already exist in the EHR functional models are identified in our profile, in order to form a “Core” for clinical research. To this core, requirements for technology and processes that would enhance the functionality will be added. The intent is to incorporate the needs of clinical research within the everyday workflow of all stakeholders. These “ease of use” requirements will be grouped into a natural

systems in clinical trials to generate and maintain source data and source documentation on each clinical trial subject. Such electronic source data and source documentation must meet the same fundamental elements of data quality (e.g., attributable, legible, contemporaneous, original, and accurate) that are expected of paper records and must comply with all applicable statutory and regulatory requirements. FDA's acceptance of data from clinical trials for decision-making purposes depends on FDA's ability to verify the quality and integrity of the data during FDA on-site inspections and audits. (21 CFR 312, 511.1(b), and 812).

progression of features to be added over time. However, only the "Core" functionality must exist in order for data from EHR systems to be suitable for regulated clinical research.

When identifying requirements for an EHR/CR, the following principles were followed:

- An EHR for Clinical Research Functional Profile will establish the requirements that identify non-redundant system functions and processes that allow the use of patient electronic medical data for clinical research.
- The use of the EHR/CR Functional Profile will ensure that data protection, patient privacy, and regulatory research requirements are met.
- Data standards are essential for data collection, interpretation and exchange within the medical and research communities. Collaboration on common data standards and data transfer standards (e.g., CDISC/HL7 joint initiative) will be critical to support both the implementation of electronic national health records for national health information networks and clinical research.
- In the EHR/CR functional profile, all functions that are described in the HL7 or EuroRec EHR Functional Models but do not relate to clinical research will be omitted. While these omitted functions may be critical to a functioning EHR system for healthcare, their omission from the EHR/CR Functional Profile only indicates that their implementation is not necessary for clinical research. EHR/CR user requirements that are not already part of the EHR Functional Models from HL7 and EuroRec will be detailed and included in the functional profiles to be submitted to these organizations for their review and endorsement

The diagram below shows, at a high level, the developing environment as it moves from core requirements for a reliable data source today toward future probable and ideal states requiring additional functionality. It illustrates the emerging and future EHR-Research connectivity as:

- A core environment that meets the minimum requirements in order to ensure the reliability of Healthcare data used for Clinical Research
- A series of future levels (labeled "Tiers") that describe an emerging environment of increasing connectivity and complexity (some of which is being piloted now).

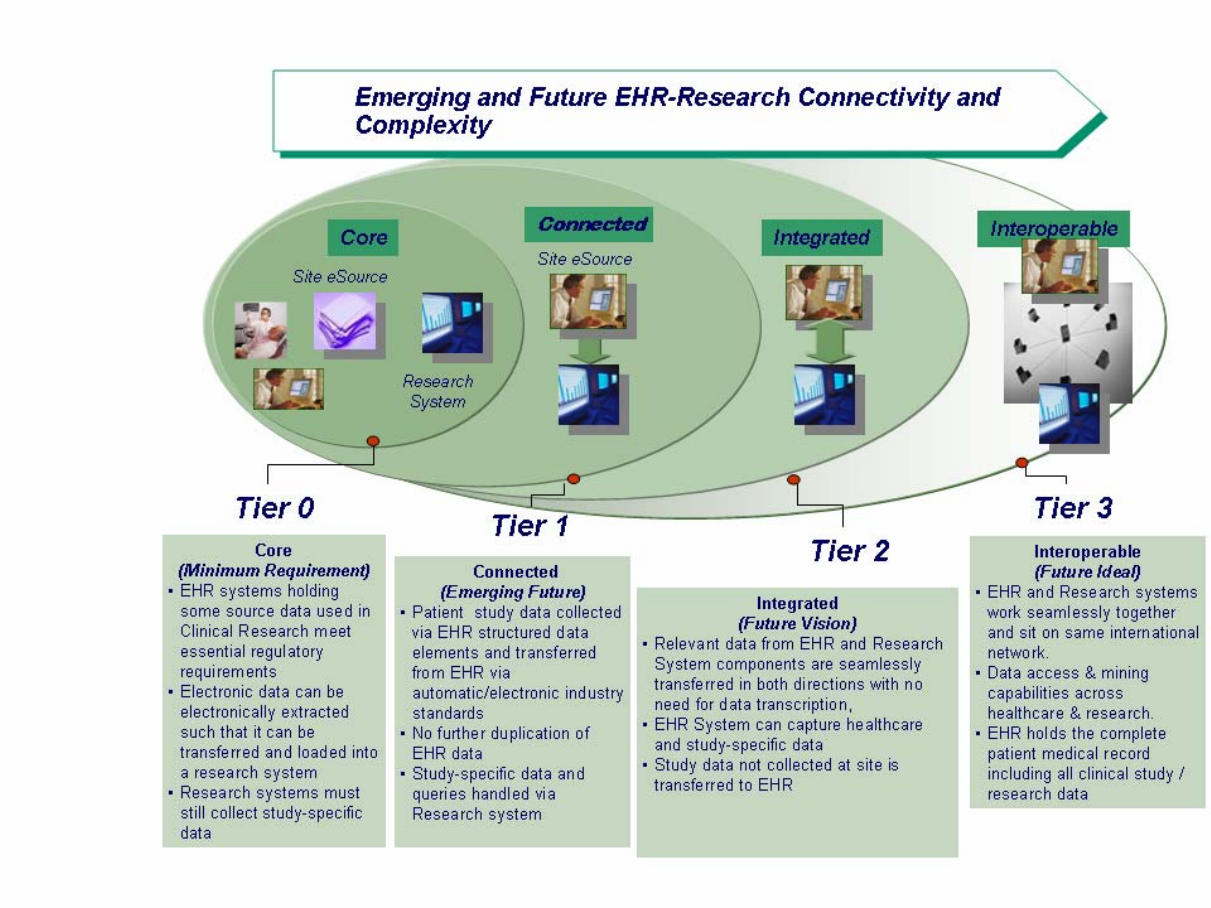

Figure 1 : Emerging and Future EHR-Research Connectivity and Complexity[3]

It is anticipated that moving from the current state of electronic health records and data capture for clinical research, to the ultimate desired state of clinical research as a natural progression of healthcare, will be a long process with many stages. Doing this in an evolutionary step-wise manner is desirable from the standpoint of easing the transition of multiple changes for system vendors, implementers and users. The evolution we are describing is a shift from a siloed environment of healthcare and clinical research, to an environment that encompasses all aspects of the health related environment. We recognize that this shift involves not just technology change, but a cultural, behavioral change as well, to where healthcare providers view research as a natural partner in their processes. At the same time, the national and international initiatives for sharing EHR data may involve not just technology solutions but cultural and behavioral shifts, and process re-designs as well. The evolution may allow the repurposing of the information to create a single virtual type of environment where healthcare data can be collected and used for dual purposes and the technical components allow the information to be sharable without incurring duplicated data entry or copying. Our vision is dependent on this paradigm shift within the healthcare industry, as in our ultimate vision, research would be viewed as one of the organizations that are serving the patient.

The remainder of this document describes only the base, or “Core” level (minimum requirements) needed to use EHR data for regulated clinical research. These requirements are based on current regulations surrounding clinical research as well as a decision of what data domains might reasonably be collected in healthcare systems. More detailed information on the EHRCR Working Group’s ideas for how the healthcare and research industries might evolve together can be found in the supplement to this document. For purposes of understanding where the healthcare and research communities are today with respect to electronic records, refer to Supplement section A2.1. This is useful pre-reading for evaluating the following discussion on Core Level Functions and Data.

[3] In this diagram, and throughout this document, the word ‘system’ may refer to a collection of systems or applications. We are not advocating any specific architecture but more that the functionality described be present in whatever set of solutions may be provided.

6. EHR/CR Core (Tier 0) Level Functions and Data

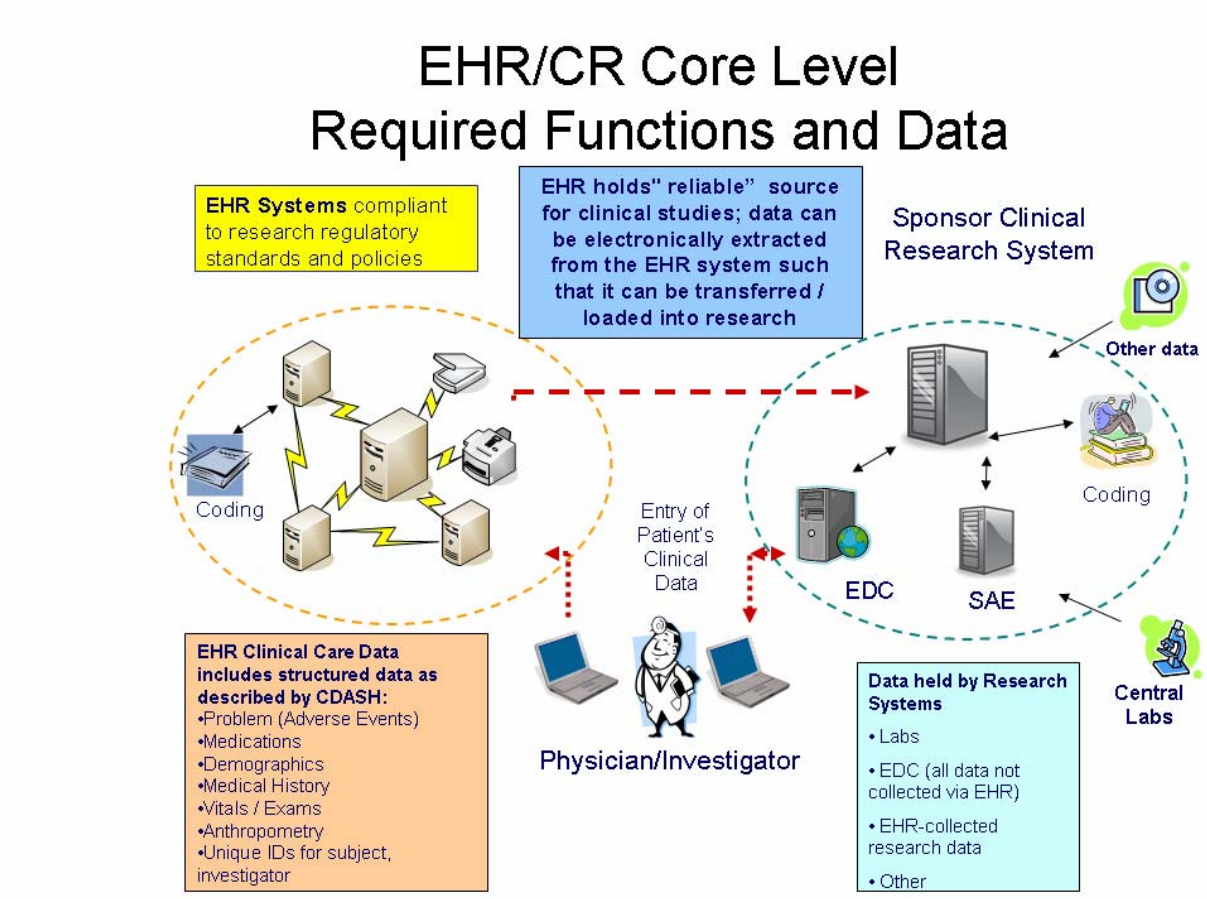

Figure 2 : Tier 0 – Core Level Functions and Data

At the "Core" level, we are proposing criteria for what determines a 'reliable' electronic data source within the healthcare environment. By achieving this level of compliance with the EHR/CR model, clinical researchers and regulators can be assured of the quality of source data that resides within the EHR systems, and their compliance with applicable regulations. This is absolutely critical as national/regional "eHealth" initiatives require more and more patient source data to be stored in these electronic systems. In the EHR/CR Functional Profile, all core requirements that are derived from regulatory requirements or guidelines (such as 21 CFR Part 11, ICH, CSUCI Guidance, HIPAA) will be identified[4].

This diagram depicts the minimal EHR requirements necessary to meet clinical research regulatory requirements in order to use source data from an EHR system for clinical research. It is expected that EHR systems that are already certified for healthcare uses (such as ambulatory care) will meet many of these requirements and beyond. The EHR systems that will meet the Core requirements for clinical research (thus complying with the requirements for an EHR/CR) will be compliant to research regulatory standards and policies through a combination of technology and process. They will hold a limited set of structured data (standard data elements and standard data terminology, such as those included in the CDISC CDASH domains (Clinical Data Acquisition Standards Harmonization). Data

[4] While the CDISC eSDI paper (see References #6) was used as a reference to help identify these requirements, it is not explicitly identified here or in the 'Source' column of the Core Requirements list (section 6.1) as this would be redundant to the reference of the actual regulatory document or guideline.

maintained in a standard / common structure can be extracted from the EHR system rather than redundantly re-entered into a clinical research system. Data being required at the Core level is data that is likely to be already maintained for a patient and/or collected during a healthcare encounter. Structured data are also required by HL7, CCHIT and EuroRec in order to share data in a meaningful way. It is not expected that all healthcare systems at this level would have clinical research-compliant data transfer facilities (such as IHE integration profiles RFD and QED) and therefore, the source data could be exported and then loaded into the research systems.

We are proposing that healthcare standards for structured patient data be harmonized such that there is semantic interoperability maintained with the CDISC standards in order to share information in a meaningful way. By doing this, the ability to participate in a clinical study is easier and more readily available to all organizations and patients who use a compliant EHR. The CDISC-HL7 relationship involves harmonizing the CDISC standards with the HL7 Reference Information Model (RIM) through the BRIDG model. The collaborative development of the BRIDG model among CDISC, HL7, FDA and NCI and other stakeholders provides a means to ensure semantic interoperability among the standards developed to support clinical research with the relevant standards for healthcare. In addition, there is an HL7-CDISC project to develop messages to carry CDISC content. These developing models and transport methods will be considered as the basis for exchange of information in future Tiers, between the EHR system and the sponsor clinical research system.

In Tier 0 (Core), we are proposing that the EHR system can capture a minimum set of structured data as recommended by the CDISC/CDASH initiative. CDISC CDASH are defining data collection standards that are applicable across therapeutic areas and research domains, regardless of differences in research sponsors. By using CDASH, the same basic set of data elements would be requested in standardized format and could be clearly defined and mapped into the EHR. In addition to standardized structured data, there must be ways to anonymize the data while maintaining unique patient identification within the clinical study.

6.1 List of Core (Tier 0) User Requirements

The table below shows high level user requirements that are necessary to achieve Core level functionality. A key goal of this level is to satisfy regulations and guidance that pertain to clinical research. To this end, we have indicated which regulatory requirements are satisfied by a user requirement. There are, however, some user requirements that are necessary to support the entire Core vision, and do not have a direct link to any regulatory requirement. Included are checkmarks to indicate whether a particular user requirement already exists in the HL7 EHR Functional Model, the EuroRec EHR Repository, the CCHIT Ambulatory Care Certification, or the CCHIT In-patient Care Certification. The HL7 EHR Functional Model and the EuroRec EHR Repository are a superset of possible EHR functionality. Individual functional profiles for specific areas (such as ambulatory care and in-patient care) are developed by subsetting criteria from these supersets. In the table below, we have indicated where our clinical research user requirements already exist in the HL7 EHR Functional Model or the EuroRec Repository. In the case where there is no direct mapping to HL7 or EuroRec, we will develop specific criteria to submit to these organizations in the HL7 and EuroRec formats. It is important to note that there are several commercial EHR systems that have passed both CCHIT Ambulatory Care and In-Patient Care certifications: a check in these columns indicates that user requirements already exist as functionality in commercial EHR systems and are being used within the healthcare arena.

Most of the following user requirements are requirements for an EHR system. Some requirements are listed as “process” as these are not requirements that can be programmed into an EHR system. These process requirements pertain to how the system is developed, maintained, and controlled both at the software developer site and at the installation site of the investigator.

Req #	Requirement Description	Source in Regs, Guidances, Standards	HL7 EHR Functional Model	EuroRec Repository	CCHIT Ambulatory	CCHIT In-patient
	Data Requirements					
C1	System can capture and maintain a minimum set of **Demographic and Subject Characteristics data** such as modeled by CDISC CDASH data collection variables for this domain.	CDISC CDASH	√	√	√	√
C2	System can capture and maintain a minimum set of **Adverse Event data** such as modeled by CDISC CDASH data collection variables for this domain (Adverse Events are indicated as ‘Problems’ or ‘Complaints’ in the HL7, EuroRec and CCHIT models)	CDISC CDASH	√	Partial	Partial	Partial
C3	System can capture and maintain a minimum set of **Medical History data** such as modeled by CDISC CDASH data collection variables for this domain.	CDISC CDASH	√	√	√	√
C4	System can capture and maintain a minimum set of **Medication data** such as modeled by CDISC CDASH data collection variables for this domain.	CDISC CDASH	√	√	√	√
C5	System can capture and maintain a minimum set of **Physical Exam** data such as modeled by CDISC CDASH data collection variables for this domain.	CDISC CDASH	√	√	√	√

Req #	Requirement Description	Source in Regs, Guidances, Standards	HL7 EHR Functional Model	EuroRec Repository	CCHIT Ambulatory	CCHIT In-patient
C6	System can capture and maintain a minimum set of **Vital Sign data** such as modeled by CDISC CDASH data collection variables for this domain.	CDISC CDASH	√	√	√	√
C7	System has the ability to capture a unique, anonymized, sponsor-provided identifier to each patient that meets data privacy requirements.	CDISC CDASH HIPAA, EU Patient Privacy laws	√	√	√	√
C8	System can capture a sponsor-provided clinical research protocol identifier and associate it with a patient					
C9	System must have the ability to capture a unique sponsor-provided site number.					
C10	System has the ability to show patient identifiers on all patient information displays including screens, images, printouts etc	CSUCI	√	Partial	√	√
C11	System has the ability to store and retrieve records in a way that is attributable to a patient (which includes associated audit trails and translation of any coded data)	Part 11, CSUCI, ICH GCP	√	√	√	√
C12	System has the ability to capture, store, update, manage, retrieve structured data		√	√	√	√
C13	System has the ability to capture, store, update, manage, retrieve unstructured data (i.e. images, free text)		√	√	√	√
C14	System has the ability for investigator to indicate which data should be exported for clinical research					
C15	System has the ability to produce a human-readable copy of data (such as hardcopy or PDF)	Part 11, CSUCI, 21 CFR 312.68, ICH GCP	√	√	√	√
	Privacy Requirements					
C16	Data can be extracted for clinical research via a recognized interchange method (will include appropriate de-identifying and only include the data points that apply to the clinical trial)	HIPAA	√	Partial		
C17	System has the ability to manage patient consent and date of consent	HIPAA, EU Patient Privacy laws	√	√	√	√

Req #	Requirement Description	Source in Regs, Guidances, Standards	HL7 EHR Functional Model	EuroRec Repository	CCHIT Ambulatory	CCHIT In-patient
C18	System has the ability for the investigator to review and mask the use of any unstructured data for clinical research such that sponsors do not review data that could inadvertently have identifying information in it.					
C19	System enables investigators to identify all patients in the EHR system who are enrolled in clinical trials at any given time and allows investigator to correlate trial-specific identifiers with such patients.		Partial		Partial	Partial
	System and Data Security Requirements					
C20	System shall have an audit trail to include recording date/time/author and reason of any data creation, change, or deletion	Part 11, CSUCI, 21 CFR 312.62	√	√	√	√
C21	System will not allow new audit trail information to over-write existing (previous) information	Part 11, CSUCI, 21 CFR 312.62	√	√	√	√
C22	System will allow review of audit trail by data point (field).	Part 11, CSUCI, 21 CFR 312.62	Partial	Partial	Partial	Partial
C23	System will limit access to audit trail and clock such that persons who create, modify, or delete patient records cannot modify the audit trail or the system clock.	Part 11, CSUCI	√	√	√	√
C24	System will limit the number of log-in attempts and record unauthorized access log-in attempts.	Part 11, CSUCI	Partial	√	√	√
C25	System will allow and enforce password or other access keys to be changed at established intervals.	Part 11, CSUCI		√	√	√
C26	System feature to allow automatic logoff or other data lock (such as password protected screen saver) after a set period of time of inactivity	CSUCI		√	√	√
C27	System should synchronize to date and time provided by international standard setting agencies (e.g. US National Institute of Standards and Technology provides information about universal time coordination (UTC))	CSUCI	Partial	√	√	√
C28	The system has the ability to create and maintain the roles, access permissions and capabilities of each user or external system that accesses the system.	Part 11, CSUCI	√	√	√	√
C30	The system will limit access to authorized users, or external systems, and ensure that such users have access only to those system features and	Part 11, CSUCI, ICH	√	√	√	√

Req #	Requirement Description	Source in Regs, Guidances, Standards	HL7 EHR Functional Model	EuroRec Repository	CCHIT Ambulatory	CCHIT In-patient
	functions to which they have been granted access.	GCP				
C31	System will allow features that restrict data viewing or manipulation to only that which is done via protective system software and which permit on-site and remote system access.	Part 11, CSUCI	√	√	√	√
C32	System will provide controls to ensure system date and time are correct, including limiting authority to making clock changes	CSUCI	Partial	√	√	√
C33	System will allow audit trail to utilize standard time-keeping method such that the local time can be derived.	CSUCI	√	√	√	√
	Process Requirements					
C34	There will be sufficient system and/or process controls for backup and recovery procedures		√	√	√	√
C35	There will be sufficient system and/or process controls to ensure that an investigator can retrieve a "certified copy" of trial data (including the audit trail) for however long the investigator has this responsibility	P Part 11, CSUCI, ICH GCP art 11	Partial	Partial		
C36	There will be sufficient system and/or process controls to prevent or mitigate effects of viruses, worms, or other harmful software code	CSUCI			√	√
C37	There will be sufficient process control for the system covering Disaster Recovery Procedures / Contingency Planning				√	√
C38	The site will have documented procedures (i.e. SOPs) for controlling user process at the site (such as login/logout procedures, system security measures (i.e. no sharing passwords), how source data are obtained and managed (including what electronic systems are used), system backup and recovery procedures, etc.)	Part 11, CSUCI				
C39	The site will have documented procedures for maintaining a copy of the source data at another location other than the clinical site	CSUCI				
C40	There will be a process to demonstrate that individuals who develop, maintain, or use the system have appropriate education, training, and experience necessary to perform their assigned task.	Part 11, CSUCI			√	√
C41	There will be a vendor process to demonstrate that development and modifications of the system use good software development lifecycle practices including documented system validation and change control such that the integrity of the data is maintained when changes are made to the	Part 11, CSUCI			√	√

Req #	Requirement Description	Source in Regs, Guidances, Standards	HL7 EHR Functional Model	EuroRec Repository	CCHIT Ambulatory	CCHIT In-patient
	computerized system, such as software upgrades, security and performance patches, equipment or component replacement.					
C42	There will be an investigator process to demonstrate that any changes to the system are documented and any required system validation and change control is performed such that the integrity of the data is maintained when changes are made to the computerized system, such as software upgrades, security and performance patches, equipment or component replacement	Part 11, CSUCI				
C43	There will be a vendor process to demonstrate that System Documentation is under change control and maintained with an audit trail.	Part 11			√	√
C44	There will be a system function and/or process to ensure the ability of the site to provide a cumulative directory of all personnel who use or access the data for the trial.	CSUCI	Partial	Partial		

Most of the requirements for clinical research already exist in the HL7 EHR Functional Model as well as the EuroRec Repository, and the CCHIT Ambulatory and In-patient certifications. In preparing the EHR/CR Functional Profile, criteria added for the Core (or "Essential Now") Level, fall into the following categories

- Research Identifiers
    - The system must have the ability to capture, store, and associate research identifiers with patients who are enrolled in clinical trials. These identifiers include subject number, protocol identifier, investigator identifier, and site identifier. These clinical-research identifiers should be included on all subject information output.

- Additional data elements
    - In addition to structured domain data already collected in an EHR system, a minimum set of additional domain data, as modeled by CDISC CDASH, are included for the following domains: Demographic, Medical History, Medication, Problem (Adverse Event), Physical Exam, Vital Signs

In order to meet clinical research regulations, the criteria in the following categories were added:

- Added privacy features:
    - Additional features for de-identifying research-bound data such that privacy regulations are met (e.g. ability to mask patient identifiers in data that will be shared with research)

- Added security features:
  - Additional security requirements (e.g. limiting number of login attempts, record failed log-in attempts, enforce periodic password change, automatic “screen lock” after a period of inactivity, limiting access to audit trail and clock, restrict data viewing)

- Added audit trail features:
  - Additional Audit trail capabilities (e.g. a method to enable local time to be derived, feature to maintain a synchronization of audit trail to master clock, ability to indicate reason for modifications, and maintenance of audit trail record after its associated patient record has been deleted)

- Produce a research-appropriate copy of data:
  - Produce human-readable copy of research-bound data and associated audit trail (e.g. in PDF or XML format)

Supplement A :

A1. Background

The focus of initiatives underway in Europe and U.S. to advance the use of electronic health records (EHRs)[5] has primarily been on healthcare delivery and until recently there has been little discussion about the needs of the pharmaceutical and allied industries[6]. However, as the use of electronic health records grows worldwide, clinical researchers are entering a new environment for documenting their research. This environment is both more complex in terms of its technological and regulatory implications and full of opportunities for improving safety, cost, and quality, while expediting the process of making new drugs available for therapy.
The environment is more complex in a number of ways. Thus far, the pharmaceutical and healthcare industries have developed electronic technologies for capturing clinical data in separate but parallel universes guided by different use cases, different regulations, different standards and different terminologies. Consequently, systems and processes put in place to support clinical research inevitably lead to duplication of effort (such as data being recorded within an electronic health record, again as an electronic research record, and frequently as a third record on paper at the site).

Currently healthcare practitioners that participate in clinical research ("investigators") are being burdened with redundant tasks that do not work with the natural flow of the clinical work processes. As the use of EHR becomes more prevalent (due to national initiatives requiring and providing incentives in this direction), the redundancy of tasks surrounding the gathering and entering of the same data, in both the healthcare system as well as the clinical research system, will increase. If the process for clinical research is not optimized to become a natural progression of patient healthcare, more and more clinicians may find it difficult to continue to participate in clinical research.

Not surprisingly, many investigators and researchers have been asking why the electronic versions cannot be linked. This would minimize data transcription and clarify some issues regarding source data. The emerging environment does, in fact, offer a tremendous opportunity to capitalize on the availability of electronic patient data. A discussion paper, "The Future Vision of Electronic Health Records as eSource for Clinical Research", written jointly by the eClinical Forum and the PhRMA EDC/eSource Taskforce describes the benefits of connecting healthcare and research (available from http://www.eclinicalforum.com).

To connect healthcare and research, three key challenges need to be addressed:

- A mechanism for satisfying regulatory and research requirements for system validation and data reliability
- Data standards for electronic data collection, exchange and interpretation
- Controlled processes for releasing and transferring data from EHR, device and research systems consistent with patient data privacy and bioethical considerations

A2. Discussion of each level of the EHR/CR Functional Profile

With this evolution of both technology and healthcare culture in mind, we have grouped the user requirements into several stages, from "Core" which is the minimum set of requirements to use data from EHR systems for regulated clinical research (this scenario working with the current cultural paradigm), to the ultimate ideal of total efficiency and multiple research uses for EHR data (using the single silo paradigm and the ability of the healthcare industry to share electronic patient data). While we are depicting an evolution from one tier to the next, in reality tiers may not be sequentially aligned or evolutionary down the path described in the following sections, but some breakthroughs and

[5] This paper is using the term "electronic health records" or EHRs to refer to an all-encompassing record that is emerging in regional and national systems. Commonly electronic records that hold individual medical information may be referred to as electronic medical records (EMRs) or electronic patient records (EPRs). Please see glossary for exact definition of EHR.
[6] The National Committee on Vital and Health Statistics (NCVHS) is in the process of developing recommendations on the secondary use of health data, which includes research, and the American Medical Informatics Association is also addressing the area of secondary use.

advance capabilities may occur in a non-linear fashion. Some of the "future state" may not be far off in the future, but pieces of it may emerge sooner than some of the other functionality that is depicted in a nearer term. That said, the following sections describe, at a high level, the required functions and data of each stage of the EHR/CR development.

To clarify the entire progression of current state to future ideal, we have included a general description of the existing situation, giving a general picture of what is available today. It does not assume that all environments have all items in the diagram or that any of the items in the diagram are usable for research.

Considering that regulations are under review and EHR development and standards are evolving, the following diagrams and text are a preliminary description of the system functions and data that may be required at each progression of the EHR/CR Functional Profile (as described in Figure 1 of the User Requirements Document) in order for an EHR system to be certified for use with clinical research at that tier level. Additionally the diagrams show items that may be handled on the research side at each tier level. Items that may currently exist (as depicted in the Current State diagram, Figure 2) may continue to exist in reality as the EHR progresses from one state to the next, however only those that are required to meet that tier level will be described and depicted in the following sections. A description of who has access to what data and functions is outside the realm of these diagrams at this time.

Prior to reading the following sections depicting a possible progression from Current State to the Future Ideal state, it might be helpful to review Section 5 of the User Requirements Document in order to put this vision in context.

A2.1 Current State of Electronic Records

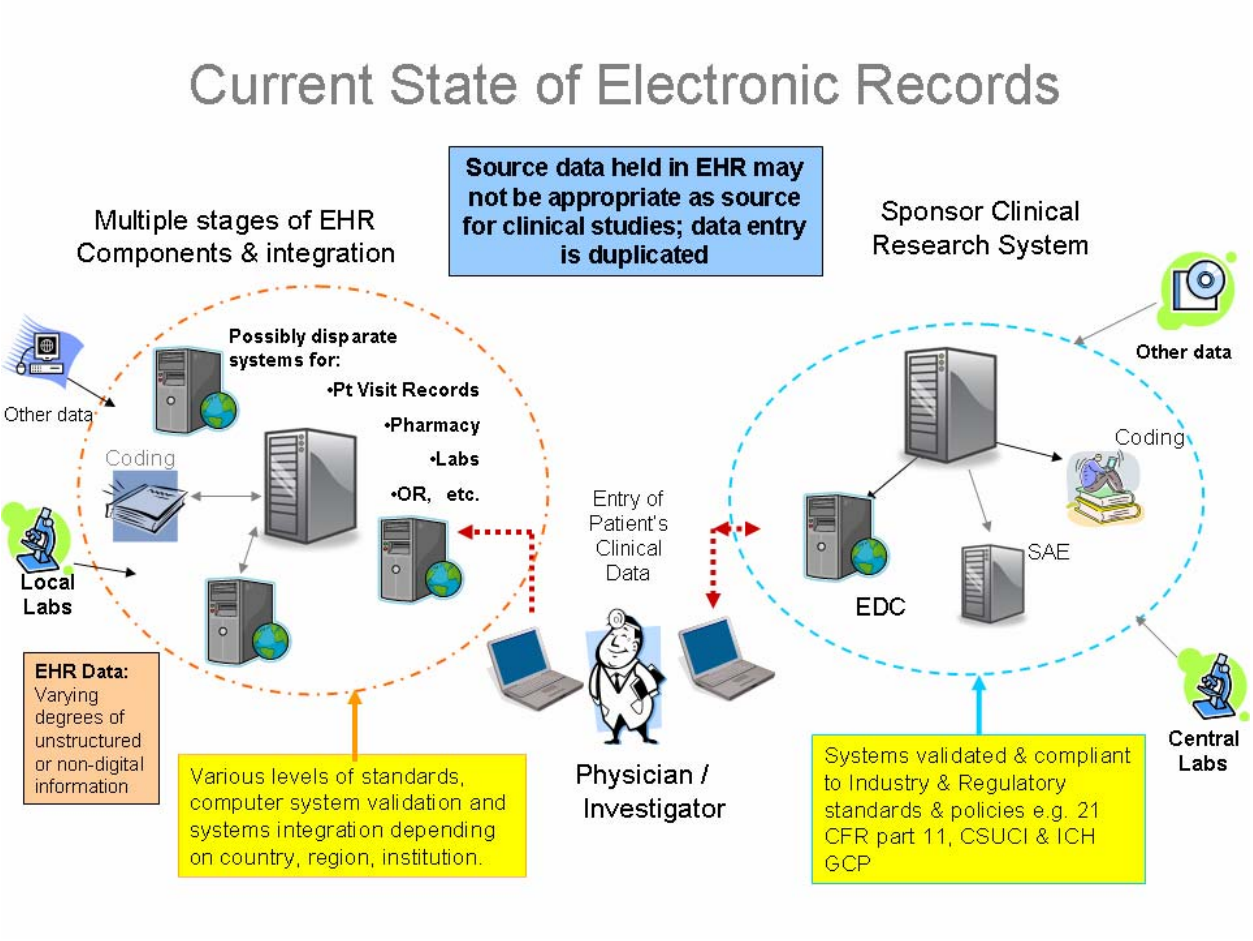

Figure 3 : Current State of Electronic Records

This diagram depicts an approximation of the current state of electronic records within the healthcare and research arenas[7]. We recognize that some healthcare organizations are much more advanced in their electronic health record implementation while others are still completely paper-based and/or using electronic records only for administrative data. Thanks to national and regional initiatives, the use of electronic records is increasing while the use of paper is becoming less prevalent. However the electronic record formats, system functionality, and associated processes are far from standard.

In the current situation, patient data are entered into both the healthcare system and the research system. This data may be similar, but the healthcare data are more likely to be unstructured (i.e. free text), while the research data will be highly structured and the systems used to capture them include quality checks to ensure their integrity. Both healthcare and research data are coded to enable other uses of the data, however the goal of each of these coding efforts differ, leading to the use of different coding classification systems. Healthcare data are likely to be stored electronically in the institution that is seeing the patient, such that one patient may have several different electronic records within different institutions and these records are likely to each have a different format, depending on the system employed by that institution. Data may be in many formats, with “other data” including ECG, imaging, x-rays, and even electronic patient questionnaires (ePRO) and IVRS (interactive voice response services). Healthcare system functionality is driven by either vendor capability or end user deployment/policy and processes aimed at efficiency in the healthcare process. Research system functionality is driven by regulatory requirements/guidance and processes aimed at efficiency in the

[7] The research system is intended to represent a separate system used for clinical research, whether the research is sponsored by the pharmaceutical industry, government grants, or self-sponsored by academic research organizations. We recognize that not all clinical research systems follow this model.

research process. Systems used to capture research data (called EDC for "electronic data capture) may be hosted by a third party in order to satisfy regulations.

A2.2 Tier 0 – Core Level

(Note to reader: this is a duplicate of section 6 in the User Requirements Document)

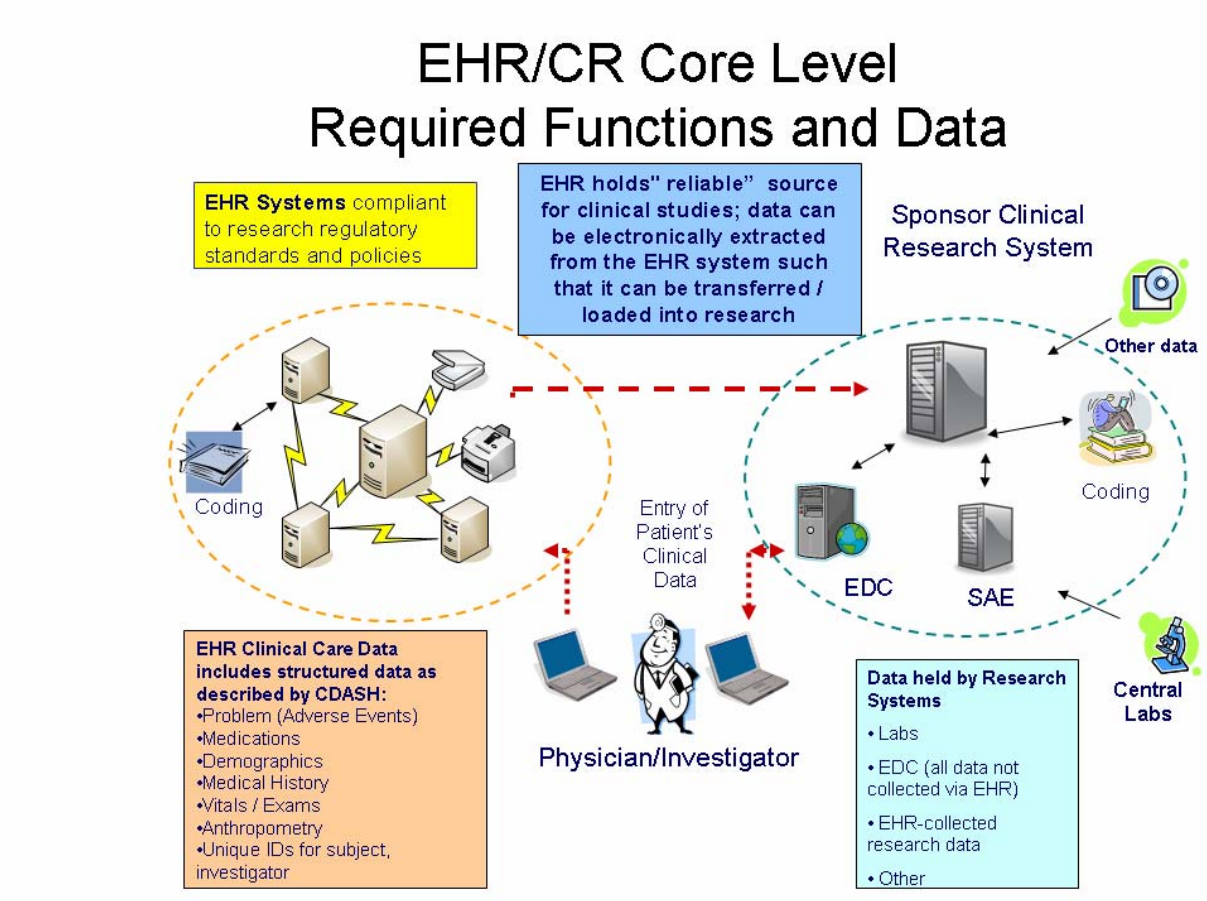

Figure 4 : Tier 0 – Core Level Functions and Data

At the "Core" level, we are proposing criteria for what determines a 'reliable' electronic data source within the healthcare environment. By achieving this level of compliance with the EHR/CR model, clinical researchers and regulators can be assured of the quality of source data that resides within the EHR systems, and their compliance with applicable regulations. This is absolutely critical as national/regional "eHealth" initiatives require more and more patient source data to be stored in these electronic systems. In the EHR/CR Functional Profile, all core requirements that are derived from regulatory requirements or guidelines (such as 21 CFR Part 11, ICH, CSUCI Guidance, HIPAA) will be identified.

This diagram depicts the minimal EHR requirements necessary to meet clinical research regulatory requirements in order to use source data from an EHR system for clinical research. It is expected that EHR systems that are already certified for healthcare uses (such as ambulatory care) will meet many of these requirements and beyond. The EHR systems that will meet the Core requirements for an EHR/CR system will be validated and compliant to industry and regulatory standards and policies through a combination of technology and process. They will hold a limited set of structured data (standard data elements and standard data terminology, such as those included in the CDISC CDASH domains(Clinical Data Acquisition, Standardization and Harmonization)) that could be used by clinical research, thus enabling this data to be extracted from the EHR system rather than redundantly entered into a clinical research system. Data being required at the Core level is data that is likely to be already maintained for a patient and/or collected during a healthcare encounter. It is not expected that all healthcare systems at this level would have clinical research-compliant data transfer facilities and

therefore, the source data can be transferred and loaded into the research systems. Structured data are also required by HL7, CCHIT and EuroRec in order to share data in a meaningful way.

We are proposing that healthcare standards for structured patient data be interoperable with the CDISC CDASH data standards in order to share data in a meaningful way. By doing this, the ability to participate in clinical study is easier and more readily available to all organizations and patients who use an EHR. The CDISC/HL7 joint initiative is an effort to harmonize CDISC data with HL7 messages. This standard, once developed, will be considered to exchange data in future Tiers, between the EHR system and the sponsor clinical research system. In addition, there must be ways to anonymize the data while maintaining unique patient identification within the clinical study. CDISC CDASH define standard data elements and terminology for all base information collected on all clinical studies, and would apply to all data used for clinical research, regardless of differences in research sponsors and therapy areas

A2.3 Secondary Uses for Core Level EHR/CR Systems

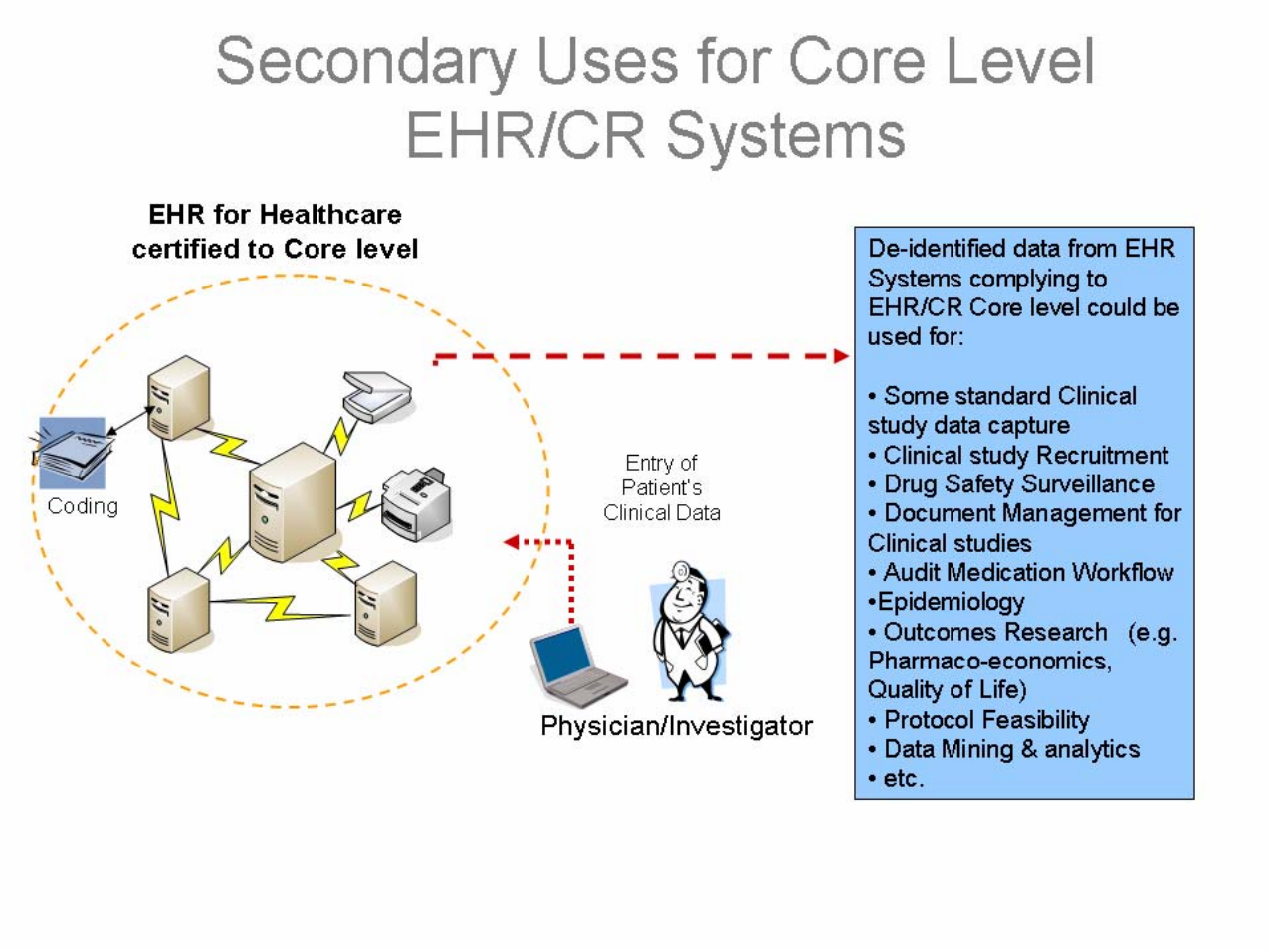

Figure 5 : Secondary Uses for Core Level EHR/CR Systems

Once "Core" competency has been reached by an EHR system, the data held in the EHR system offers uses for a broad range of research purposes, including those listed in the diagram above. Therefore, by meeting some basic criteria/ functionality, the value of the data in the EHR systems will increase even before most of the data can be exchanged/ integrated directly with research systems (such as EDC electronic data capture systems). Such value is already being realized by

Cleveland Clinic[8] and the Holston Medical Group[9] in matching patients for clinical studies utilizing existing EHR systems. Retrospective studies are being conducted with the GPRD[10] that consist of approximately 10 million patients in the UK, to study patient outcomes and adverse events. With the further adoption of EHR, it will then be possible for prospective studies enabling cohort studies and monitoring the long-term health outcomes of patients managing their chronic or acute conditions. Utilizing EHRs for secondary use such as clinical study recruitment is already occurring, as well as epidemiology studies utilizing GPRD. By implementing basic criteria and functionality into future EHR development and implementations, much greater value can be realized from the broader health information exchange opportunities that exist.

A2.4 Tier 1 – Connected (Emerging Future)

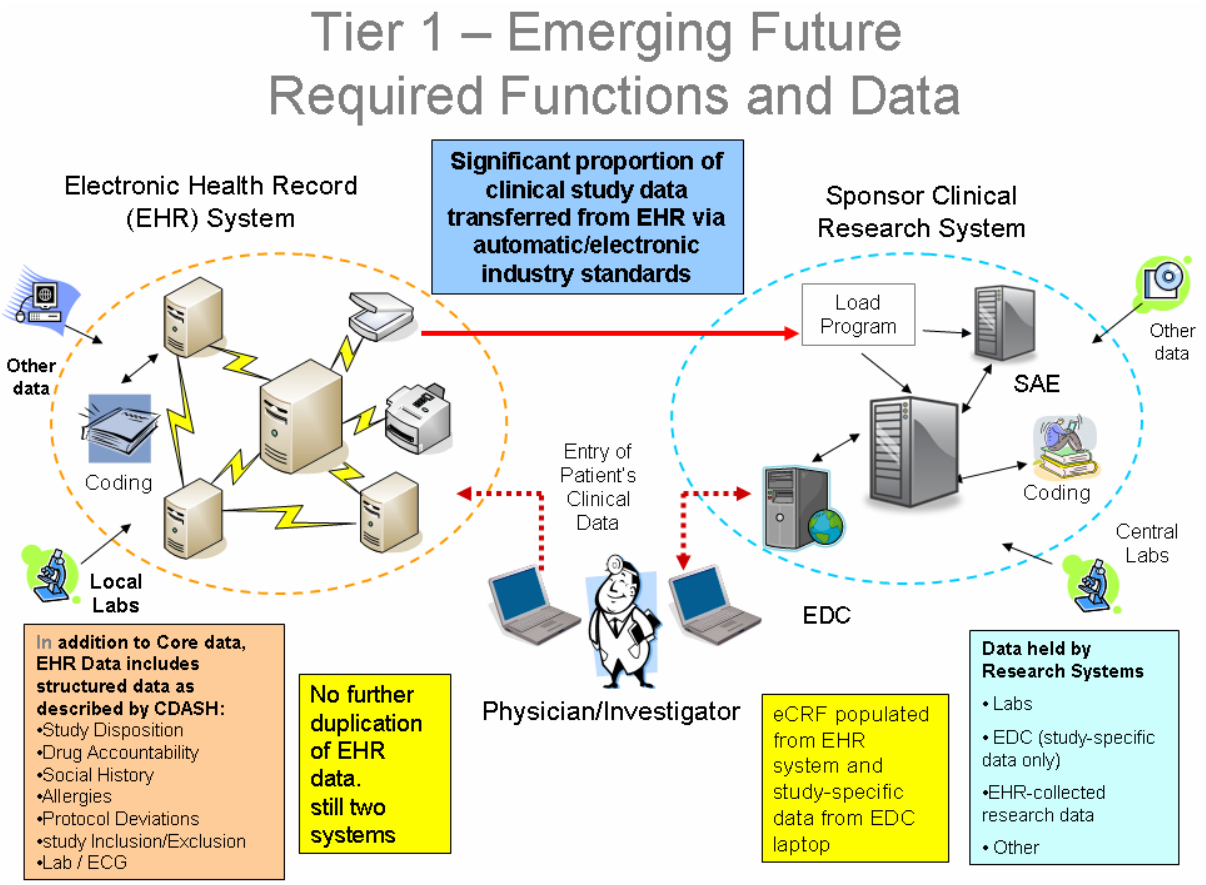

Figure 6 : Tier 1 – Emerging Future

At the Tier 1 level, the EHR is expanded to include all standard data required for all clinical studies (i.e. all data, except that which is study-specific and not otherwise typically recorded in a clinical encounter outside of clinical research), and this data can be transferred from the EHR to the research system through technology that meets industry standards for security and reliability. At this point, no data that

[8] Embi, PJ, Jain, A, Clark, J, Bizjack, S, Hornung, R. Harris, M, "Effect of a Clinical Trial Alert System on Physician Participation in Trial Recruitment", Archives of Internal Medicine VOL 165, OCT 24, 2005

[9] AllScripts case study, located at http://www.allscripts.com/siteresources/files/casestudies/The%20EHR%20Solution%20to%20Clinical%20Trial_Holston%20Case%20Study.pdf; last accessed July 15, 2007

[10] GPRD – General Practitioners Research Databse - http://www.gprd.com/intro/default.asp

is routinely entered into the healthcare system would need to be redundantly entered/transcribed into the research system, thus optimizing investigator processes. Only study-specific data would be entered through a research EDC system. The EDC system or other research system will be needed to validate the data and communicate data queries to the investigator as the electronic transfer mechanism at the Tier 1 level is unidirectional. Since the healthcare system is now collecting all the standard research data, the EHR record has now become the repository of the patients' source data used in clinical studies thus maintaining investigator control without need for any third party handling of data (as is the case when source data are entered into a research system). Study-specific data is still collected and held via a research system.

A2.5 Tier 2 – Integrated (Future Vision)

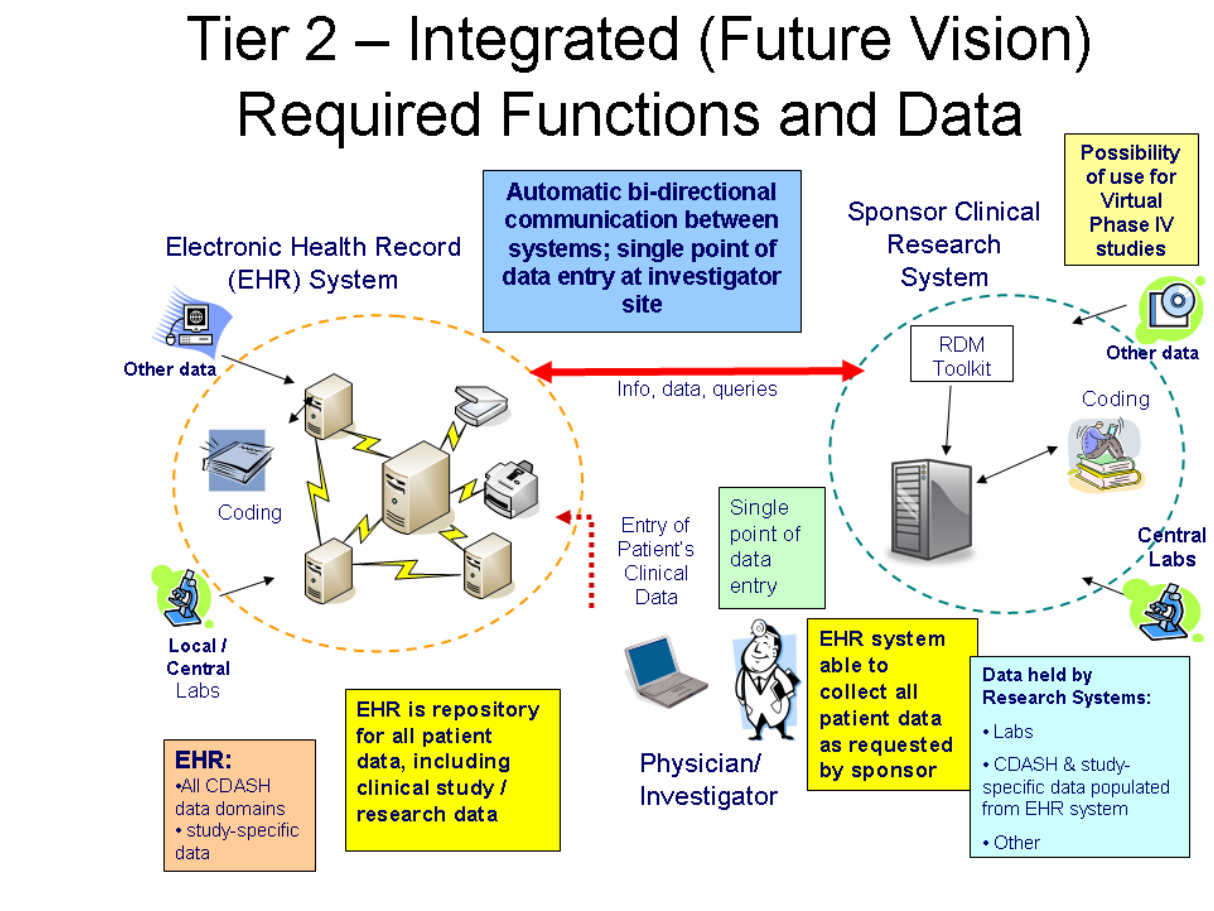

Figure 7 : Tier 2 – Integrated (Future Vision)

At the Tier 2 level, *all* the patient data (including study-specific data) for a clinical study is collected via the EHR system, and data information transfer is bi-directional (data going to research, queries going to EHR), thus completely eliminating the need for a research EDC system at the site and making participation in clinical studies more available. Study data not collected at the site is transferred to the EHR (shown in diagram as "Other Data"[11]). A program will be necessary on the research system to perform functions such as Data loading, Query Management[12], data validation checking, consistency checks, data aggregation, database lock, SAE (serious adverse event) data

[11] If research systems are used to collect any study source data, the data would still need to be handled separated via a 3rd party prior to transfer to the EHR.

[12] While Query Management is a common process in the current as well as Tier 1 scenarios where much of the data is transcribed, thus producing a large number of data queries, in this scenario it is greatly reduced since the research sponsor is now getting eSource data. However, note that there will always be a need to discuss and track issues with the investigator, so the Query Management function will always be needed.

management, etc. (labeled as "RDM (research data management)Toolkit" in the diagram above). Since all data will originate with the healthcare system, there is no need for data reconciliation between two separate databases (in particular, Serious Adverse Event (SAE) data, that now undergoes a stringent data reconciliation process, would no longer require this as SAE data would be handled the same as all other research data via the RDM Toolkit). All phases of clinical research (I to IV) can be performed through the EHR and the clinical data from these will be stored on the EHR and available for physicians to review with all other historical data on a patient for the lifetime of the patient.

A2.6 Tier 3 – Interoperable (Future Ideal)

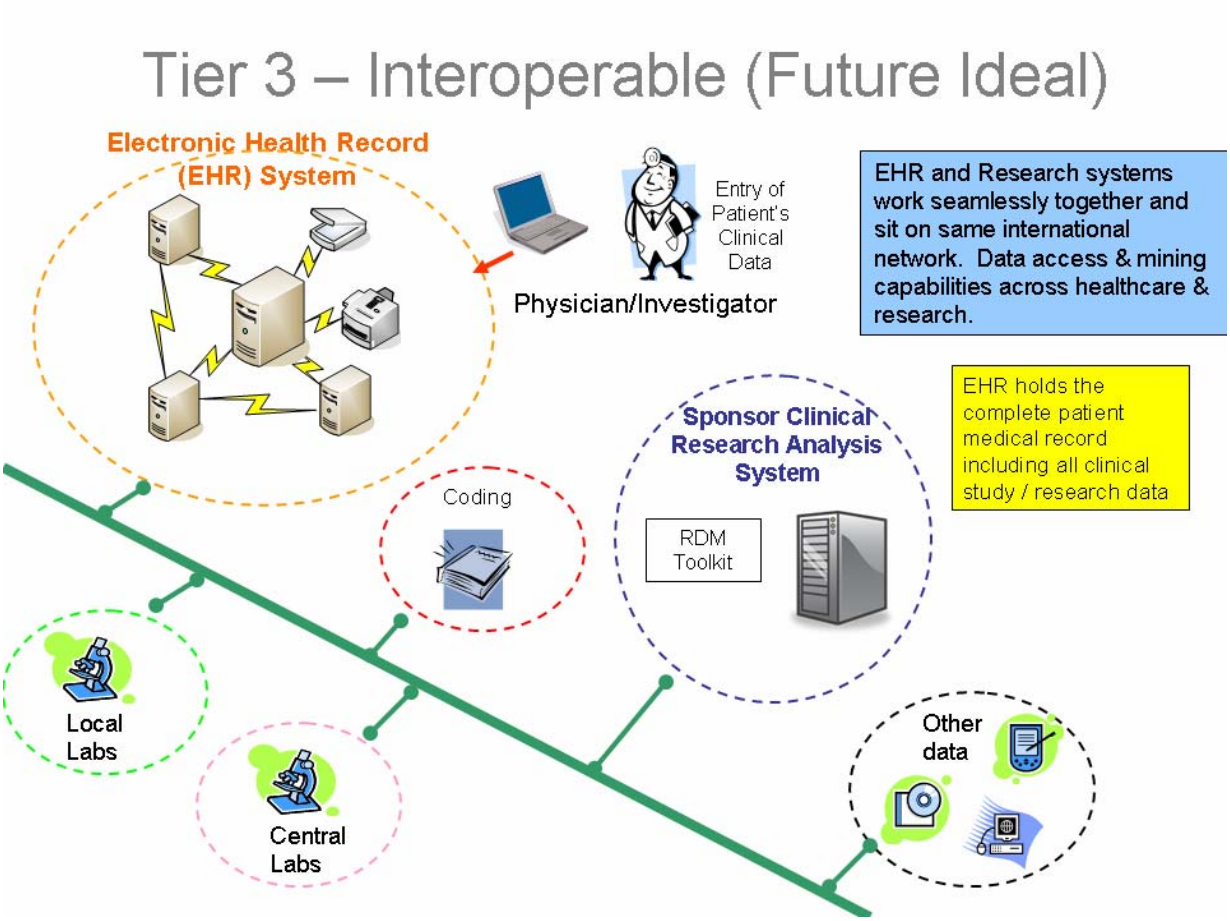

Figure 8 : Tier 3 – Interoperable (Future Ideal)

Tier 3 is a Future Ideal. We recognize that this may be many years away, but it is necessary to keep our eyes focused on the desired end result. In the Future Ideal state, EHR and research systems work seamlessly together so that stakeholder groups benefit from data access and mining capabilities across healthcare and research data sets. Research systems and healthcare systems sit on the same international network and conform to the same data and data exchange standards. There is no longer the need to move research data into an EHR system as the research data are just another node on the network. This allows a subject's data to be pulled together from data held in healthcare and research. Data mining across all patients' data are possible. Programs could be developed to allow for virtual Phase IV studies.

In this future ideal, the following scenarios are possible …

- Phase I data held uniquely in research but now being referenced by EHR for the subject and included as part of the patient record
- Research being able to “test run” eligibility criteria to assess a protocol's chances of achieving the planned enrollment rate.
- Authorities could obtain all SAE information for all past study patients and would be able to aggregate experiences over extended periods of time**.**

APPENDIX 1: Future Tier (Non-Core) User Requirements

The table below shows high level user requirements that might be necessary to achieve the future functionality (Tiers 1 through 3) as described in sections A2.4, A2.5, and A2.6. This is a fairly thorough, but not exhaustive list, primarily based on criteria already existing in the HL7 EHR Functional Model and/or CDISC CDASH and electronic signature requirements from 21 CFR Part 11. Completing this list, determining what tier each requirement would support, and mapping them to HL7 and EuroRec criteria is part of Phase II of this project.

Req #	Requirement Description
	Data Requirements
F1	System can capture and maintain **Inclusion / Exclusion** data as modeled by CDISC CDASH data collection variables for this domain.
F2	System can capture and maintain **Demographic data** as modeled by CDISC CDASH data collection variables for this domain.
F3	System can capture and maintain **Subject Characteristics** data as modeled by CDISC CDASH data collection variables for this domain.
F4	System can capture and maintain **Medical History and Substance Use** data as modeled by CDISC CDASH data collection variables for this domain.
F5	System can capture and maintain **Medication** data as modeled by CDISC CDASH data collection variables for this domain.
F6	System can capture and maintain **Laboratory and ECG** data as modeled by CDISC CDASH data collection variables for this domain.
F7	System can capture and maintain **Physical Exam** data as modeled by CDISC CDASH data collection variables for this domain.
F8	System can capture and maintain **Study Medication** data as modeled by CDISC CDASH data collection variables for this domain.
F9	System can capture and maintain **Study Disposition** data as modeled by CDISC CDASH data collection variables for this domain.
F10	System can capture and maintain **Protocol Violations** using a coding list
F11	System must define, capture and maintain **Visit / Study Event** Identifier as defined by protocol visit/event schedule.
	Data Management Requirements
F12	System can use standard information models (such as CDISC CDASH formats)
F13	Ability to extract CDASH data elements
F14	Ability to capture CDASH data elements
F15	Ability to apply data validation checks and warnings to data capture mechanism. Mechanism should not allow automatic entry of data when a field is bypassed but may allow repopulation of data that has previously passed data validation check.
F16	Ability to produce a report/listing of the data (both structured and unstructured) including information of how it changed over time
F17	System can assist with the coding of diagnoses, procedures and outcomes based on information entered into the system during a patient visit
F18	System can generate customized reports or views via set-up or import of trial-specific report formats
F19	System can generate standard reports or views via set-up or import of trial-specific report formats
F20	System can organize patient data by encounter or visit
F21	Ability to produce a “certified copy” of data in PDF or XML format (or other currently acceptable format)
F22	Ability to produce a data archive
	Privacy Requirements
F23	System can support secure communication to protect the privacy of information as required by federal or jurisdictional law.

Req #	Requirement Description
F24	System allows secure data exchange for extracting data for clinical research or importing data into the EHR system (via standards-based encryption / decryption mechanisms or other acceptable method for obfuscation.)
F25	System will de-identify the associated audit trail as appropriate for clinical research
F26	System will allow automated "opt in" tracking indicating patient has consented for use of data in clinical research (whether or not patient is on a clinical trial)
F27	Data can be extracted for clinical research via a recognized interchange standard (will include appropriate de-identifying as per local legal requirements and only include the data points that apply to the clinical trial)
	System Communication Requirements
F28	System will use recognized interchange standards to provide a standard export mechanism
F29	System can use standard terminology to communicate with other (internal & external) systems
F30	System will have method to maintain, version, and cascade changes for standard terminologies
F31	System will provide the ability to capture and/or accept patient data from remote devices and integrate that data into the patient's record
F32	System will accept and append patient encounter data from external systems, such as diagnostic tests and reports
F33	System will provide two-way electronic communication between investigator and sponsor
F34	System will provide two-way electronic communication between investigator and clinical trials patient and/or the patient representatives
F35	Ability to alert investigator if patient's data is updated anywhere it is stored
F36	Ability to automatically update patient demographic information through interaction with other systems, applications and modules
F37	Ability to support exchange of information between providers as part of the patient care process, and the appropriate documentation of such exchanges.
F38	System will provide features to enable secure bidirectional communication of information electronically between practitioners and pharmacies or between practitioner and intended recipient of pharmacy orders.
F39	Ability to facilitate electronic access to educational or support resources pertinent to, and usable by, the patient or patient representative.
	Terminology Standards Requirements
F40	System can support terminology mapping (map one terminology to another)
F41	System can use a hierarchical approach to search data via the standard terminologies
F42	System can interoperate with other systems which are using different terminology versions
F43	System can assist with the coding of diagnoses, procedures and outcomes based on information entered into the system during a patient visit
	Process Flow Requirements
F44	System will allow Process and Data rules to be created, updated, viewed, deleted and used to direct system behavior (e.g. Online maintenance of the clinical research protocol)
F45	System allows for rules to be created, updated, viewed, deleted and used to assist site staff in protocol related decision-making (e.g. does patient need a protocol test according to protocol schedule, should the patient recruitment be notified to the sponsor, should the sponsor be notified about an SAE, are the data points within the range, etc.)
F46	System allows for rules to be created, updated, viewed, deleted and used to assist site staff in protocol related diagnosis (e.g. which patients are potential candidates for the clinical trial, does the patient meet inclusion exclusion criteria, system can scan the medication list and the knowledge base to see if any of the symptoms are side effects of medication already prescribed as well as possible complications / diagnoses, system can identify potential Adverse Events / Problems or trends.)
F47	System allows for rules to be created, updated, viewed, deleted and used to assist site staff in controlling the protocol process flow (e.g.

Req #	Requirement Description
	presents appropriate screens to collect relevant information for the visit, directs incoming sponsor queries to appropriate staff, reminds the study personnel of trial-specific procedures that need to be ordered.)
F48	System allows for rules can be created, updated, viewed, deleted and used to controlling access privileges to data and functionality (e.g. based on the role of the user can they access/modify a data point, view the audit trail, access data export functions)
F49	System allows for rules related to a clinical trial protocol to be exported (e.g. as a record for sponsor, for purposes of system validation)
F50	Ability to alert the clinician to drug-drug, drug-allergy, and drug-food interactions at levels appropriate to the health care setting and with respect to the patient condition. These alerts may be customized to suit the user or group.
F51	System allows clinical study protocol-specific scheduling is incorporated into patient scheduling function of the EHR
F52	System can offer prompts to support the adherence to care plans, guidelines, and protocols at the point of information capture.
F53	System to provide warnings for clinical trial protocol violations
F54	System will identify trends that may lead to significant problems, and provide prompts for consideration
F55	System will identify drug interaction warnings at time of medication ordering.
F56	Identify and present appropriate dose recommendations based on known patient-conditions and characteristics at the time of medication ordering
F57	System should provide recommendations and options in medication and monitoring on the basis of patient diagnosis, cost, local formularies or therapeutic guidelines and protocols
F58	System will track tasks to facilitate monitoring for timely and appropriate completion of each task
F59	System will offer prompts based on patient-specific data at the point of information capture for assessment purposes
F60	System will support the integration of patient and family preferences into clinical decision support
F61	System will identify and present the appropriate care plans, guidelines and/or protocols for the management of patient specific conditions that are identified in a patient clinical encounter.
F62	System allows assignment, delegation and/or transmission of tasks to the appropriate parties
	Electronic Signature Requirements
F63	System shall have the ability to have an investigator electronically sign an electronic record
F64	System allows electronic signatures to contain a printed name of the signer, date and time of signature execution, and meaning of the associated signature.
F65	System allows electronic signatures to be associated or linked to its respective electronic record.
F66	System allows electronic Signatures to be unique to an individual
F67	System allows electronic signatures not to be based on Biometrics shall use two distinct identification code and password on the first signature in a session, and at least one of the distinct elements for subsequent signatures, and the signature can only be used by the owner
	Registry and Directory Requirements
F68	System provides the ability for secure and appropriate use of registries and directories.
F69	System allows registry to hold information such that all a patient's medical information from any originator can be identified and retrieved.
F70	System allows directories can be used to identify which sites may have patients appropriate for a clinical trial, or to provide a means to do retrospective data mining to identify trends in medication uses, prescribing habits, general population adverse experiences, etc.
F71	System allows investigators to use directories to find sponsors of clinical trials

Req #	Requirement Description
F72	System allows communication between EHR systems and registries and directories through standardized interfaces.
F73	System allows Clinical Researchers to add, change, or export data in directories and registries as appropriate.
F74	System allows investigator to produce a list of all patients enrolled in clinical trials
F75	System allows context-sensitive output interfaces
F76	System provides support for academic research (note: this is very vague and needs to be further refined in a future release of this document).

APPENDIX 2: Core (Tier 0) Level User Requirements mapped to EN Criteria

For those wishing to also review the EHR-CR Functional Profile, Release 1, the following mapping between Core (Tier 0) User Requirements and the HL7 EHR-CR Functional Profile EN (Essential Now) functions/criteria is provided.

Req #	Requirement Description	Source in Regs, Guidances, Standards	DC Profile	Supportive Profile	Info Infrastr Profile
	Data Requirements				
C1	System can capture and maintain a minimum set of **Demographic and Subject Characteristics data** such as modeled by CDISC CDASH data collection variables for this domain.	CDISC CDASH	DC.1.1.2.1(all)	S.1.3.1 (1,2)	
C2	System can capture and maintain a minimum set of **Adverse Event data** such as modeled by CDISC CDASH data collection variables for this domain (Adverse Events are indicated as 'Problems' or 'Complaints' in the HL7 and EuroRec models)	CDISC CDASH	DC 1.2 .1(4) DC 1.4.1(all) DC.1.4.4.1(all)		
C3	System can capture and maintain a minimum set of **Medical History data** such as modeled by CDISC CDASH data collection variables for this domain.	CDISC CDASH	DC.1.2.1(all) DC.1.4.1(all)		
C4	System can capture and maintain a minimum set of **Medication data** such as modeled by CDISC CDASH data collection variables for this domain.	CDISC CDASH	DC.1.4.3(all) DC.2.3.1.1(all)		
C5	System can capture and maintain a minimum set of **Physical Exam data** such as modeled by CDISC CDASH data collection variables for this domain.	CDISC CDASH	DC.1.5(all)		
C6	System can capture and maintain a minimum set of **Vital Sign data** such as modeled by CDISC CDASH data collection variables for this domain.	CDISC CDASH	DC.1.8.4.1(all)		
C7	System has the ability to capture a unique, anonymized, sponsor-provided identifier to each patient that meets data privacy requirements.	CDISC CDASH	DC.1.1.1.1(5, 13-18)	S.1.4	

C8	System can capture a sponsor-provided clinical research protocol identifier and associate it with a patient		DC.1.1.1.1(5,13,16) DC.2.2.1.1(1,2)		
C9	System must have the ability to capture a unique sponsor-provided site number.		DC.1.1.1.1(18)		
C10	System has the ability to show EHR patient identifiers on all patient information displays including screens, images, printouts etc	CSUCI	DC.1.1.1.1 (15) DC.2.2.1.1(1)		
C11	System has the ability to store and retrieve records in a way that is attributable to a patient (which includes associated audit trails and translation of any coded data)	Part 11, CSUCI, ICH GCP	DC.1.1.1.1(all) DC.2.2.1.1(1,2)		
C12	System has the ability to capture, store, update, manage, retrieve structured data				IN.2.5.2 (all)
C13	System has the ability to capture, store, update, manage, retrieve unstructured data (i.e. images, free text)				IN.2.5.1 (all)
C14	System has the ability for investigator to indicate which data should be exported for clinical research				IN.1.8(12)
C15	System has the ability to produce a human-readable copy of data (such as hardcopy or PDF)	Part 11, CSUCI, 21 CFR 312.68, ICH GCP			IN 2.1 (8)
	Privacy Requirements				
C16	Data can be extracted for clinical research via a recognized interchange method (will include appropriate de-identifying and only include the data points that apply to the clinical trial)	HIPAA			IN.1.8(11,12) IN.2.4.1(all)
C17	System has the ability to manage patient consent and date of consent	HIPAA, EU Patient Privacy laws	DC.1.3.1(all)		
C18	System has the ability for the investigator to review and mask the use of any unstructured data for clinical research such that sponsors do not review data that could inadvertently have identifying information in it.				IN.1.8(12)
C19	System enables investigators to identify all patients in the EHR system who are enrolled in clinical trials at any given time and allows investigator to correlate trial-specific identifiers with such patients.		DC1.1.1.1(15, 16) DC.2.2.1.1(all)	S.1.4	
	System and Data Security Requirements				
C20	System shall have an audit trail to include recording date/time/author	Part 11,			

	and reason of any data creation, change, or deletion	CSUCI, 21 CFR 312.62			IN.2.2.1 (3-7,17)
C21	System will not allow new audit trail information to over-write existing (previous) information	Part 11, CSUCI, 21 CFR 312.62			IN.2.2.1 (8,9,12)
C22	System will allow review of audit trail by data point (field).	Part 11, CSUCI, 21 CFR 312.62			IN.2.2.1 (12)
C23	System will limit access to audit trail and clock such that persons who create, modify, or delete patient records cannot modify the audit trail or the system clock.	Part 11, CSUCI	DC.2.2.1.1		IN.1.3(5)
C24	System will limit the number of log-in attempts and record unauthorized access log-in attempts.	Part 11, CSUCI			IN.1.1.1(4)
C25	System will allow and enforce password or other access keys to be changed at established intervals.	Part 11, CSUCI			IN.1.1.1(5)
C26	System feature to allow automatic logoff or other data lock (such as password protected screen saver) after a set period of time of inactivity	CSUCI			IN.1.1.1(6)
C27	System should synchronize to date and time provided by international standard setting agencies (e.g. US National Institute of Standards and Technology provides information about universal time coordination (UTC))	CSUCI			IN 2.2.1(14)
C28	The system has the ability to create and maintain the roles, access permissions and capabilities of each user or external system that accesses the system.	Part 11, CSUCI, ICH GCP			IN.1.2(1,3-6) IN.6.2(1,2)
C30	The system will limit access to authorized users, or external systems, and ensure that such users have access only to those system features and functions to which they have been granted access.	Part 11, CSUCI, ICH GCP			IN.1.2 (6) IN.1.3 (4)
C31	System will allow features that restrict data viewing or manipulation to only that which is done via protective system software and which permit on-site and remote system access.	Part 11, CSUCI			IN.1.3(6)
C32	System will provide controls to ensure system date and time are correct, including limiting authority to making clock changes	CSUCI			IN.1.3(5) IN.2.2.1(13-16)
C33	System will allow audit trail to utilize standard time-keeping method such that the local time can be derived.	CSUCI			IN.2.2.1(4)

	Process Requirements				
C34	There will be sufficient system and/or process controls for backup and recovery procedures				IN.2.2.2(6-9)
C35	There will be sufficient system and/or process controls to ensure that an investigator can retrieve a "certified copy" of trial data (including the audit trail) for however long the investigator has this responsibility	Part 11, CSUCI, ICH GCP			IN.2.1(1,5) IN.2.4.2(5)
C36	There will be sufficient system and/or process controls to prevent or mitigate effects of viruses, worms, or other harmful software code	CSUCI			IN.1(1)
C37	There will be sufficient process control for the system covering Disaster Recovery Procedures / Contingency Planning				
C38	The site will have documented procedures (i.e. SOPs) for controlling user process at the site (such as login/logout procedures, system security measures (i.e. no sharing passwords), how source data are obtained and managed (including what electronic systems are used), system backup and recovery procedures, etc.)	Part 11, CSUCI			
C39	The site will have documented procedures for maintaining a copy of the source data at another location other than the clinical site	CSUCI			
C40	There will be a process to demonstrate that individuals who develop, maintain, or use the system have appropriate education, training, and experience necessary to perform their assigned task.	Part 11, CSUCI			
C41	There will be a vendor process to demonstrate that development and modifications of the system use good software development lifecycle practices including documented system validation and change control such that the integrity of the data is maintained when changes are made to the computerized system, such as software upgrades, security and performance patches, equipment or component replacement.	Part 11, CSUCI			
C42	There will be an investigator process to demonstrate that any changes to the system are documented and any required system validation and change control is performed such that the integrity of the data is maintained when changes are made to the computerized system, such as software upgrades, security and performance patches, equipment or component replacement	Part 11, CSUCI			
C43	There will be a vendor process to demonstrate that System Documentation is under change control and maintained with an audit trail.	Part 11			IN 2.2.2(4)
C44	There will be a system function and/or process to ensure the ability of the site to provide a cumulative directory of all personnel who use or	CSUCI		S.1.2.1(all)	IN.1.2(8)

	access the data for the trial.				

APPENDIX 3: Project Participants

The Electronic Health Records for Clinical Research project is under the organization of the eClinical Forum and PhRMA EDC/eSource Taskforce. Participants are from the pharmaceutical, healthcare technologies, and clinical research technologies industries, and federal regulatory bodies. Open communication and coordination with both HL7 Technical Committee and EuroRec are ongoing. The project is funded through contributions from the pharmaceutical industry.

EHR/CR Functional Profile Working Group Co-chairs

John D. Mestler	Procter & Gamble Pharmaceuticals, PhRMA EDC/eSource Taskforce, eClinical Forum
Suzanne Bishop	SKB Consulting, eClinical Forum US
Richard Perkins	ConSept Consulting, eClinical Forum EU
Catherine Célingant	Millennium Pharmaceuticals, Inc., PhRMA EDC/eSource Taskforce, eClinical Forum

EHR/CR-FP Functional Profile Working Group (International Group)

Marie MacDonald	Astellas US LLC
Gary Drucker	Bayer Healthcare, Pharmaceuticals
Tricia Gregory	Boehringer Ingelheim Pharmaceuticals
Darlene Kalinowski, M.S.	Bristol Myers Squibb
Jane Griffin, RPh	Cerner Corporation (EHR vendor)
David Stein	ClinPhone Inc (Clinical technology vendor)
Ian Hamilton	Eli Lilly & Company
Linda King	Eli Lilly & Company
Vicente Rodriguez	Eli Lilly & Company
Jay Levine	FDA
Armando Oliva	FDA
Joe Salewski	FDA
Susan Howard	Glaxo SmithKline Pharmaceuticals
Frank Jensen	Lundbeck Pharmaceuticals, EFPIA
John Speakman	NIH / Cancer Research Foundation
Harry Greenspun, M.D.	Northrop Grumman Health Solutions
Mitra Rocca	Novartis Pharmaceuticals
Mathias Poensgen	Nycomed GmbH
Tiina Hartikainen	Orion Pharma
Daijin Kim	Pfizer Pharmaceuticals
Miguel Valenzuela	Roche Products Limited

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APPENDIX 4: Glossary

CCHIT	US Certification Commission for Healthcare Information Technology
CDASH	CDISC standard: Clinical Data Acquisition Standards Harmonization
CDISC	Clinical Data Interchange Standards Consortium
Certification	A quality labeling process provided by an independent, unbiased, professional and trustworthy organization that will indicate that a system has met a specific set of criterion.
Certified Copy	(From US FDA Guidance for Industry: Computerized Systems Used in Clinical Investigations) A certified copy is a copy of original information that has been verified, as indicated by a dated signature, as an exact copy having all of the same attributes and information as the original.
Clinical trial	Any investigation in human subjects intended to discover or verify the clinical, pharmacological, and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.
ECG	Electrocardiogram
EDC	Electronic Data Capture (system used for entering clinical research data at investigator sites)
EHR	Electronic health record
EHR/CR FP	Functional profile for describing functionality needed to conduct clinical research via an EHR system
ePRO	Electronic Patient Reported Outcomes (e.g. using a handheld device, IVRS, etc.)
EuroRec	European Institute for Health Records (network of National ProRec centres throughout Europe to promote adoption of electronic healthcare records. ProRec centres provide certification of EHR systems.)
FDA	US Food and Drug Administration
HL7	Health Level Seven Standards Organization
Investigator	A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.
IVRS	Interactive Voice Response System used for patient randomization, patient diary (patient-reported outcomes), etc.
Q-REC	European Quality Labeling and Certification of Electronic Health Record Systems
Research Protocol	(Also called Clinical Trial Protocol) A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guidance, the term protocol refers to protocol and protocol amendments.
SAE	Serious Adverse Event (SAE) : Any untoward medical occurrence that: • Results in death, • Is life-threatening, • Requires inpatient hospitalization or prolongation of existing hospitalization, • Results in persistent or significant disability/incapacity, or • Is a congenital anomaly/birth defect. (From the ICH guidance for Clinical Safety Data Management: definitions and Standards for Expedited Reporting.)
Sponsor	Clinical research sponsor (e.g. bio-pharmaceutical company)
System	(From US FDA 21 CFR Part 11 Glossary of Terms) Computer Systems

Validation	Validation: Confirmation by examination and provision of objective evidence that computer system specifications conform to user needs and intended uses, and that all requirements can be consistently fulfilled.

APPENDIX 5: References

1. Privacy Laws
   - U.S. FDA. 45 CFR Parts 160 and 164. HIPAA: Health Insurance Portability and Accountability Act (1996) including the Standards for Privacy of Individually Identifiable Health Information (2004). http://www.hipaadvisory.com/regs/finalprivacy/
   - EU Directive 95/46/EC of the European Parliament on the protection of individuals with regard to the processing of personal data and on the free movement of such data (1995), http://www.cdt.org/privacy/eudirective/EU_Directive_.html

2. Regulations
   - U.S. FDA 21 CFR Part 11 Electronic Records; Electronic Signatures Final Rule (1997), http://www.fda.gov/ora/compliance_ref/part11/FRs/background/pt11finr.pdf
   - ICH (International Conference on Harmonisation), FDA, E6 Good Clinical Practice: Consolidated Guidance", (1996). http://www.fda.gov/cder/guidance/959fnl.pdf
   - U.S. FDA 21 CFR Part 212 Investigational New Drug Application (Revised April, 2006), http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm?CFRPart=312

3. Guidances
   - U.S. FDA Guidance for Industry, Computerized Systems Used In Clinical Investigations (CSUCI) (May 2007); http://www.fda.gov/cder/guidance/7359fnl.pdf
   - U.S. FDA,. Guidance for Industry, Part 11, Electronic Records; Electronic Signatures - Scope and Application (2003). http://www.fda.gov/cder/guidance/5667fnl.htm

4. Standards Development Organizations
   - Health Level 7 (HL7): http://www.hl7.ca
   - Clinical Data Interchange Standards Consortium (CDISC): http://www.cdisc.org
   - Joint CDISC / HL7 Charter: http://www.cdisc.org/single_source/about.html

5. EHR Certifying Bodies
   - CCHIT – Certification Commission for Healthcare Information Technology: http://www.cchit.org
   - EuroRec – European Institute for Health Records (EuroRec): http://www.eurorec.org/
   - Q-Rec – European Quality Labeling and Certification of Electronic Health Record Systems, http://www.eurorec.org/projects/qrec.cfm?actief=q-rec

6. Other References
   - CDISC eSDI, Leveraging the CDISC Standards to Facilitate the use of Electronic Source Data within Clinical Trials, (2006), http://www.cdisc.org/eSDI/eSDI.pdf

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- AllScripts case study, located at http://www.allscripts.com/siteresources/files/casestudies/The%20EHR%20Solution%20to%20Clinical%20Trial_Holston%20Case%20Study.pdf;
- GPRD – General Practitioners Research Databse - http://www.gprd.com/intro/default.asp
- National Committee on Vital and Health Statistics, Enhanced Protections for Uses of Health Data: A Stewardship Framework for “Secondary Uses” of Electronically Collected and Transmitted Health Data (Oct, 2007), http://www.ncvhs.hhs.gov/071031lt.pdf