Electronic Health Records/Clinical Research
EHRCR Functional Profile Working Group

EuroRec Electronic Health Records
for Clinical Research
Functional Profile, Version 1.0
January 2010

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Preface

Notes to Readers

The present document describes a Functional Profile that identifies critical capabilities for the conduct of regulated clinical research utilizing EHR systems. Further to conforming to the EuroRec Repository Profiling Tools, this Profile identifies additional functionalities toward facilitating ease of use for those involved in clinical research.

The submission was finalized in October 2009 and formally approved by EuroRec on November 2009.

EHRCR Functional Profile Working Group

The EHRCR Functional Profile Working Group is comprised of dedicated individuals from the United States and the European Union in the following industries: pharmaceutical, biotechnology, clinical research technology vendor, healthcare technology vendor, and federal regulator. Decisions made by this team (as specified in the EHRCR User Requirements Document, Release 1) were reviewed and commented on by an international group of key stakeholders. Their opinions have been taken into consideration while formulating this functional profile. More information on the workings of this project team can be found at www.ehrcr.org.

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Realm

While this profile was developed within the EuroRec context, it is appropriate for both the US and EU as it is based on regulations from both arenas. We feel that it is highly applicable to any setting (including non-US and non-EU) in which clinical research is being performed. We recognize that in these settings it may be applicable to modify the language used to describe potential users of the system. The EHRCR Functional Profile Working Group invites feedback and participation from other standards development organizations, as well as clinical research stakeholders from any part of the world in which clinical research is being performed.

1. EHR/Clinical Research (EHRCR) Functional Profile: Introduction

The EHRCR Functional Profile is intended to provide high-level requirements necessary for using electronic health record data for regulated clinical research, and to further provide a roadmap toward an evolutionary process of integrating the environment that provides both patient care and data for clinical research. This functional profile is aimed at encouraging EHR vendors and developers to incorporate functions into their products that are necessary to utilize the Electronic Health Records as a direct data source for clinical studies. It is intended to provide one overall view of the needs of regulated clinical research with respect to electronic patient records.

The EHRCR project is aimed at developing a Functional Profile that identifies critical capabilities for the conduct of regulated clinical research utilizing EHR systems. Our efforts establish conformance to the EuroRec Repository Profiling Tools. We have developed a set of requirements for using EHR systems in the conduct of regulated clinical research. These requirements have been mapped into this functional profile and identify those portions of the EuroRec Repository statements that apply to **B23 Clinical Trials and Research**, thus providing EHR vendors and Investigative Sites with conformance criteria that are specific to regulated clinical research in the EuroRec formats.

2. Background (EuroRec-EHRCR EU Sub-team Working Group)

Through an invitation from the HL7 EHR Technical Committee in October 2006, the global EHRCR Functional Profile working group was organized in December 2006 by the eClinical Forum and the PhRMA EDC/eSource Taskforce, both not-for-profit professional associations supporting bio-pharmaceutical research. EuroRec fortuitously joined the effort, so that Pharmaceutical Research subject matter experts from both sides of the Atlantic were invited to come up with a global proposal to expand and adapt the functionality of EHR and associated systems, networks, and processes to support clinical research. The first set of 31 Clinical Research User Requirements was finalized early in 2008 and provided the basis for both the HL7 EHRCR Functional Profile and the present sister EuroRec EHRCR Functional Profile.

Founded in 1994, the EUROREC Institute (EuroRec) is an independent not-for-profit organization, promoting in Europe the use of high quality Electronic Health Record systems (EHRs). One of its main missions is to support, as the European certification body, EHRs quality labeling and defining functional and other criteria.

EuroRec is organised as a permanent network of National ProRec centers and provides services to industry (the developers and vendors), healthcare providers (the buyers), policy makers and patients. More information on EuroRec can be found at www.eurorec.org.

The EHRCR Working Group is a collaborative effort between the bio-pharmaceutical and healthcare industries and associated vendors and regulators, having members from each of these stakeholder groups as active participants. The first deliverable of this group was a User Requirements Document, released to stakeholders for comment in November 2007, with Release 1 in February 2008. This document outlines the basic approach of this group and provides a mechanism for broad feedback on user requirement, which was used to refine the EHRCR

Functional Profiles. Release 2 of this document was finalized in January 2010. More information on the EHRCR Working Group, as well as the User Requirements document, can be found at www.ehrcr.org.

The first EHRCR Functional Profile which maps User Requirements specifically to conformance criteria for EHR systems was submitted to HL7, went through extensive review and a formal balloting process, to become an HL7 Normative Standard in January 2009 and an ANSI Standard in July 2009.

In parallel, a European sub-team closely worked for over a year with EuroRec and mapped the same User Requirements to the EuroRec EHR conformance clauses (Fine Grained Statements), which led to the creation of the sister EHRCR EuroRec Profile - publically announced in November 2009. The full EHRCR working group strongly believes that a potential approval by CEN and inclusion of the EuroRec Profile to its standards, further to filling a currently indentified need for system developers and auditors for the European member states, will undoubtedly constitute a huge step forward for the global efforts in attaining interoperability between EHRs and Clinical Research: it definitely paves the way for and gets global healthcare stakeholders closer to a single international EHRCR Standard.

While the EHRCR working group operates independently from the Joint Initiative Council/Joint Working Group, the consistent approach in defining and releasing both Profiles is fully aligned and embraces the proceedings and philosophy of the ISO led harmonization efforts. The EHRCR proposed standards and processes are based on and referencing the work of the SDOs involved in ISO TC215 (HL7, CDISC, EN13606) whose input is directly and promptly sought.

3. Why this profile is needed

Electronic Health Records are viewed by government agencies, payers, epidemiologists as well as the clinical research community as a quantum step forward in meeting their respective needs. The current EHR environment can be described as on the rise and accelerating in its importance and adoption priority. The expansion and government-encouraged use of EHR systems in hospitals and physician offices means that patient data are increasingly being maintained electronically. Within Europe, the use of EHRs varies greatly among countries but in some areas is nearing 100%. Use in the US is on the rise, with recent reports suggesting that 25%-37% of US healthcare practices use electronic medical/health record systems.   There has been significant media attention given to the national efforts of the European Union (EU) and US to develop Nationwide Health Information Networks (NHINs). It is appropriate to consider *now* how clinical research can utilize these healthcare systems and avoid redundant collection of data, while complying with government regulations.

The Pharmaceutical and Biotech industry has made significant progress in the execution of regulated clinical studies. This has, in part, been the result of advances in the collection of patient data. The traditional paper-based clinical studies (utilizing paper case report forms) have given way to systems that support Electronic Data Capture (EDC) of clinical research data. Advances in information technology with regard to regulatory compliant software applications, telecommunications and more importantly the internet, has enabled clinical research data to be collected and reviewed in near "real-time". It is estimated that a third of regulated clinical research is conducted using EDC systems, and this too is on the rise. Currently however, data must be transcribed into the EDC system from a variety of sources. These include paper-based patient records and those maintained in Electronic Health Records (EHR) systems that may be in use at the investigational site (i.e., hospitals, doctors' offices, clinics, etc). This constitutes a duplication of effort for the study site personnel and raises the potential error rate.

Neither EDC nor EHR systems have all that is required to serve the purposes of the other (i.e., healthcare or regulated clinical research). In the case of regulated clinical research, the research sponsor must not have exclusive control of the investigator's patient data. Regulatory agencies want to ensure that data cannot be compromised either accidentally or intentionally. Therefore, the investigator must hold the source (independent of the sponsor's database and not under the sponsor's control). Additionally, investigators are required to maintain accurate case histories for

each of their patients. Increasingly, the investigational sites that are conducting clinical trials using sponsor-supplied EDC systems also have EHR systems that require input of some of the same patient data. The result is often the creation of a third record of information, on a paper copy that is printed from the EHR system. This paper copy may be used to transcribe information into the EDC system and placed in the patient's file to satisfy a regulatory requirement for source data verification, thus adding the burden to maintain paper files to the investigational site. With a sponsor provided EDC system, the trial data must either be printed out or provided electronically to the investigator to maintain once the clinical study has finished. This duplication of data and the tasks related to entering, maintaining and archiving result in costs which will grow with the increasing use of electronic data sources (i.e., through the progress of national initiatives to create an eHealth environment in which all patient health records will be electronic).

While a solution might be to use data directly from EHR systems for regulated clinical research purposes, this cannot be done at this time. The number of different systems and architectures make it difficult, if not impossible to integrate with EDC systems on anything greater than a one-to-one integration, which is not economically feasible. Many EHR systems do not have ways to either integrate or export data. Data in these systems are often unstructured (i.e., textual as opposed to data fields to collect individual, identifiable data items). Additionally, EHR systems are not controlled by clinical research regulations. As stated above, the result is often the creation of a third record of information (either via paper or an investigator-controlled, regulatory-compliant eSource system) to meet regulations. Thus, initiatives toward building standards are critical to the future success of this effort.

The International Conference on Harmonisation (ICH) provide requirements for clinical trial records, and the systems and processes that maintain them and several other guidance documents complement the existing legislation and constitute the regulatory context (e.g. FDA Guidance: Computerized Systems Used in Clinical Investigations (CSUCI) and FDA Title 21 Code of Federal Regulations (CFR) Part 11), EudraLex Volume 4, Annex 11 "Computerized Systems", EMEA/GCP Inspectors WG Reflection Paper on Expectations for Electronic Source Documents used in Clinical Trials): The same responsibilities of the investigator toward the accuracy of source data exists whether that data is hand-written on paper or entered and stored electronically. If data are entered and stored into an EHR or EDC system as the sole source and used in regulated clinical research, then that system must be compliant with these regulations (for example, data in EHR / EDC systems that are used as eSource for clinical trials, under current regulation, require authority checks such as ensuring that only authorized persons can access the system and maintaining a clinical research-compliant audit trail).

Healthcare in general is under tremendous time and cost pressures. Patient records predominantly serve the purpose of the medical care of the patient and are optimized toward this purpose. It would be inefficient and costly for a hospital or physician's office to carry out the meticulous documentation that is common in the bio-pharmaceutical industry unless the EHR system is designed to handle those tasks "behind the scenes".

The ideal environment then provides non-redundant systems and processes that allow the use of patient electronic health data for clinical research in a way that meets data protection, regulatory, and ethical research requirements and minimizes the challenges of clinical research for healthcare professionals. This environment would include regulated clinical research in the natural workflow of a clinical practice thus providing tremendous benefit (to all stakeholders) with minimal impact to the healthcare provider.

As EHRs become more widely utilized and more sophisticated, healthcare providers will begin to seek functionality that will add value beyond the core functions related to the provision of healthcare. The secondary use of healthcare data for quality reporting, quality improvement, outcomes assessment, and research will become a vital part of standard medical practice. Healthcare providers will eventually require EHRs that support and facilitate these functions and EHR vendors will need to respond.

For more information on this topic, this group recommends a discussion paper prepared by the eClinical Forum and PhRMA EDC/eSource Taskforce ("*The Future Vision of Electronic Health*

Records as eSource for Clinical Research", September 14, 2006) that can be downloaded from www.ehrcr.org (under Documents). While this paper is now several years old, it is still a relevant discussion on the benefits to patients, healthcare providers and clinical research, by connecting healthcare and research.

4. Project Details:

4.1. Scope and Methods

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 nation/region healthcare providers, may not be feasible or essential at this point. 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.

The EuroRec EHR for Clinical Research Functional Profile (EHRCR) has been created by direct entry of the 31 Tier 0 Core User Requirements within the EuroRec Repository and their mapping to 91 Fine Grained Statements (mostly pre-existing but there were new ones proposed by the EHRCR working group that have been approved and integrated by EuroRec). The Fine Grained Statements pertaining to Regulated Clinical Research are grouped under a specifically allocated Care Setting (**B23**, Clinical Trials and Research). The same Clinical Research User Requirements have been mapped to HL7 Conformance Criteria in the sister EHRCR HL7 Functional Profile.

Most of the EuroRec EHRCR Fine Grained Statements naturally predated the Clinical Research User Requirements and had been indexed under several other Care Settings (from General Practice to Tertiary Care Specialist Hospitalizations). The same Fine Grained Statements serve different Business Functions and describe Component Types ranging from EHR System functionalities to Investigative Site Process requirements. Further to their primary function of certifying EHR systems, they could therefore be used effectively to check (e.g. Audits / Inspections / Clinical Research Monitoring) for system and process implementation at the Sites, in line with Regulatory Requirements currently in effect.
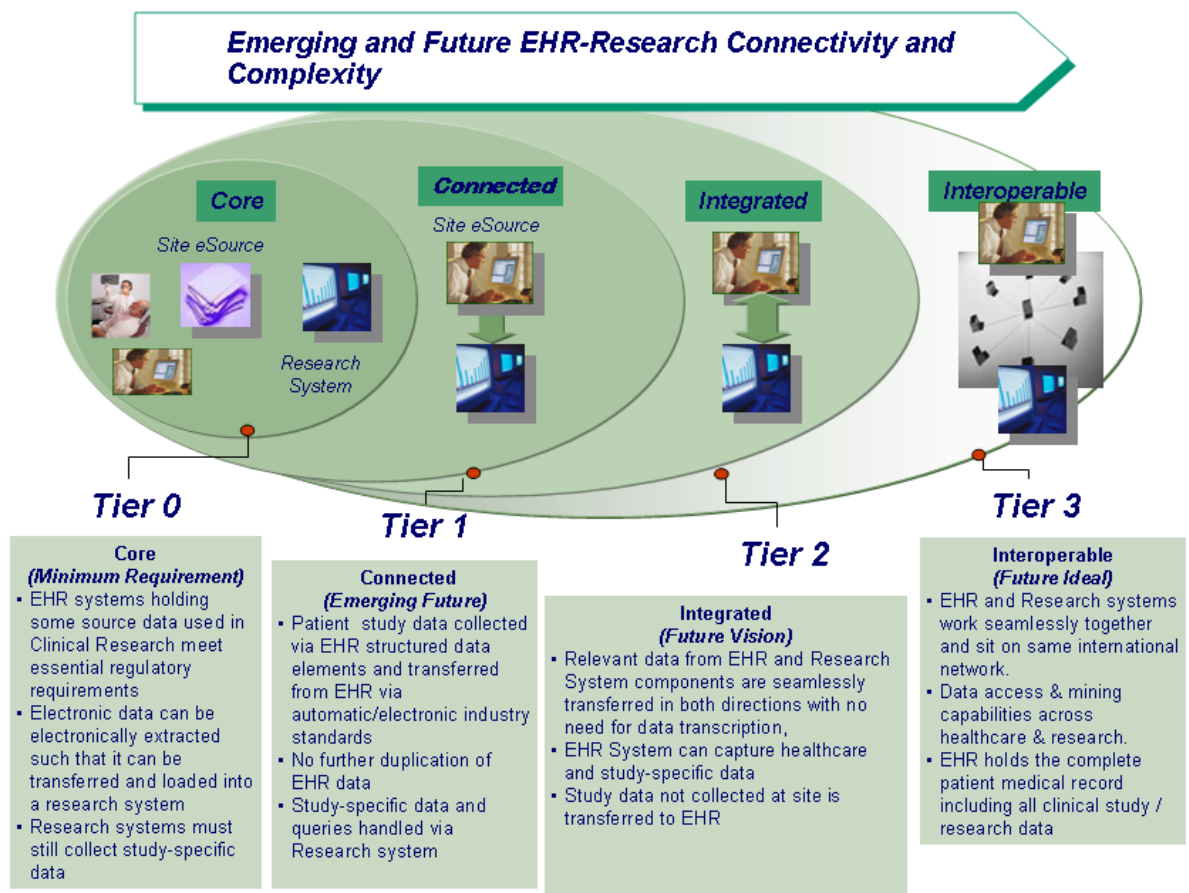
In both EHRCR Functional Profiles (HL7 and EuroRec), such features are being grouped into tiers showing a natural progression of features to be added over time. The "Tier 0" functionality that must exist in order for data from EHR systems to be reliable Source data for regulated clinical research, are contained in Section 7.0 of the present document.

When identifying requirements for an EHRCR, the following principles were followed:
- An EHR for Clinical Research Functional Profile establishes the requirements that identify system functions and processes that allow the use of patient electronic medical data for regulated clinical research.

- The use of the EHRCR 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 (including EHR narratives) and data transfer standards will be needed to support both the implementation of electronic national health records for national health information networks and clinical research. Both EHRCR Functional Profiles will endorse those standards as they become viable.

- In the EHRCR functional profile, all functions that are described in Fine Grained Statements but do not relate to clinical research have not been included. While these functions may be critical to a functioning EHR system for healthcare, their omission

from the EHRCR Functional Profile only indicates that their implementation is not necessary for clinical research.

- Tier 0 requirements that make up the Core include a minimum set of data for clinical research. This is basic information (which includes data relating to the safety of the product) that would be collected for all clinical trials, and is based on CDISC CDASH (Clinical Data Acquisition, Standardization and Harmonization Version 1.0, October 2008) "highly recommended" elements. The EHRCR Working Group believes this is a good starting-point for providing usable data for Clinical Research in an EHR system. We believe this is a stepping stone for protocol-specific data requirements (both safety and those that vary by trial and typically relate to the effectiveness of the product) that will be part of Tiers 1-3 described below. The CDASH "highly recommended" data elements have been listed in this profile's fine grained statements; CDASH modeling has not been required and is listed as a reference. Tier 0 requirements are generic enough to be considered stable regardless of future amendments to the CDASH standard (or adoption of alternative data acquisition standards). They can be expressed into data structures that meet the Electronic Submission requirements in the EMEA and FDA (e.g. ICH eCTD Specification v.3.2, FDA/CDER eCTD Submissions, EMEA EudraLex - Volume 2B - eCTD)
- The use of the data after it leaves the EHR and is moved into research is not part of this profile. While we are aware that in some cases there is integration with research EDC system, this profile does not imply that this is an expected or sought-after scenario.

Emerging and Future EHR-Research Connectivity and Complexity

Tier 0	Tier 1	Tier 2	Tier 3
Core *(Minimum Requirement)* • EHR systems holding some source data used in Clinical Research meet essential regulatory requirements • Electronic data can be electronically extracted such that it can be transferred and loaded into a research system • Research systems must still collect study-specific data	**Connected** *(Emerging Future)* • Patient study data collected via EHR structured data elements and transferred from EHR via automatic/electronic industry standards • No further duplication of EHR data • Study-specific data and queries handled via Research system	**Integrated** *(Future Vision)* • Relevant data from EHR and Research System components are seamlessly transferred in both directions with no need for data transcription, • EHR System can capture healthcare and study-specific data • Study data not collected at site is transferred to EHR	**Interoperable** *(Future Ideal)* • EHR and Research systems work seamlessly together and sit on same international network. • Data access & mining capabilities across healthcare & research. • EHR holds the complete patient medical record including all clinical study / research data

4.2 Interoperability

The EHRCR Core Functionality is primarily focused on patient data collection and management. These may be provided by a collection of systems or applications, or provided by a single system or application provided by a single vendor.

All components, modules, or applications within an EHR system used to support regulated clinical research should respond to users in a well-integrated fashion. Thus, each component, module or application must be interoperable to the degree required by the certification, documentation or procurement quality specifications (as described in EuroRec Use Tools) and specified in this profile. ISO 20514 states: "*The key to interoperability is through standardization of requirements for the EHR (record) architecture (e.g. ISO/TS 18308:2004) and ultimately the standardization of the EHR architecture itself (e.g. ENV 13606-1:2008)".*

The EHRCR Profile Project has used CDISC (SDTM and CDASH) Standards as a reference for determining data elements required for this version for the EHRCR Functional Profile.

CDISC is a globally recognized Standards Development Organization with a published process. CDISC holds Liaison A Status with ISO TC 215 for healthcare standards and is a member of the Joint Initiative Council (JIC) along with HL7, ISO, CEN and IHTSDO.

CDASH (Clinical Data Acquisition Standards Harmonization) is a content standard that identifies a core set of information (case report form fields) required across clinical studies and shares the controlled terminology (codesets) with SDTM (Study Data Tabulation Model) the predominant Standard for Regulatory Submissions in both sides of the Atlantic.

The CDISC Standards Development Process (COP-001) includes three review cycles: a) across CDISC standards teams, b) within the Critical Path Initiative Collaborative Group organizations, and c) a broad global public review that generated comments from numerous countries including but not limited to the ICH regions of Europe, Japan and the U.S. and also China. All comments were addressed. CDISC Standards are openly published at http://www.cdisc.org/standards/ .

Clinical Research Glossary

The following is a glossary of terms that are specific to clinical research and have been used in this functional profile:

CDASH	CDISC standard: Clinical Data Acquisition Standards Harmonization (see reference for link to website)
CDISC	Clinical Data Interchange Standards Consortium
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) (including procedure(s) and devices(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.
Consent Form	A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a paper or electronic signed and dated informed consent form.
CRF	Case report form (CRF): A printed, optical, or electronic document designed to record all of the research protocol required information to be reported to the sponsor on each trial subject.
EDC	Electronic Data Capture (system used for entering clinical research data at investigator sites)
eCRF	Electronic Case report form (eCRF): An electronic document designed to record all of the protocol-required information to be reported to the sponsor on each trial subject.
EHR-S	Electronic health record system
EHRCR FP	Functional profile for describing functionality needed to conduct clinical research via an EHR system
EUROREC	European Institute for Health Records
ePRO	Electronic Patient Report Outcomes (e.g. using a handheld device, IVRS, etc.)
HIMSS	Health Information Management Systems Society
HIPAA	US Health Insurance Portability and Accountability Act, includes the *Standards for Privacy of Individually Identifiable Health Information (Privacy Rule)*
HITSP	Health Information Technology Standards Panel (US): produces "Interoperability Specifications" that harmonize and recommend the technical standards necessary to assure the interoperability of electronic health records and help support the nationwide exchange of healthcare data.
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceutics for Human Use (see Reference section)
IHE	IHE ("Integrating the Healthcare Enterprise") is an international organization by healthcare professionals and industry to improve the way computer systems in healthcare share information by focusing on the development of global standards and on the regional deployment of interoperable products. IHE aims to create a process through which interoperability can be implemented. The group gathers case requirements, identifies available standards, and develops technical guidelines that manufacturers can implement.
Inclusion / Exclusion Criteria	Criteria used to select subjects for participation in a clinical trial. These include general health attributes that may require the subject to be in good health or have a disease for which the investigational drug is targeted. Inclusion / exclusion criteria also includes question regarding allergies, medication that prohibited or those required for entry into the clinical trial. Childbearing potential is normally included as well.
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.
Investigational Product	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further

	information about an approved use.
IVRS	Interactive Voice Response System used for patient randomization, patient diary (patient-reported outcomes), etc.
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 or medical device company)
Subject number	A unique number that is assigned to a subject during the course of a clinical trial. This number is used so that the subject's identity can be is not divulged.
21 CFR Part 11	FDA: Electronic Records, Electronic Signatures; Final Rule-- Criteria for acceptance by FDA under certain circumstances of electronic records, electronic signatures, and handwritten signatures executed to electronic records as equivalent to paper records and handwritten signatures executed on paper.
Source Statement/Reference Statement	(EuroRec Repository): Formalized statements of requirement, functional specifications, conformance criteria or test plans that apply in whole or in part to EHR systems and preferably have been used within at least one jurisdiction, or at minimum have been subject to a formal peer review process (such as a ballot).
Fine Grained Statement	(EuroRec Repository): Decompositions of the Source/Reference Statements into one or more specific and singularly focused clauses (or sub-clauses). Fine Grained Statements must be unambiguous and granular.
Good Practice Requirement	(EuroRec Repository): Aggregations of similar or complementary EuroRec Fine Grained Statements across multiple sources, which constitute richer and broader requirements, functional specifications and conformance criteria that apply to EHRs.

5. Overview of Added Criteria Critical to Clinical Research

Most of the requirements for clinical research already existed in the EuroRec Repository. In preparing the EHRCR Functional Profile, criteria added for the "Tier 0" Level, fall into the following categories:

- Research Identifiers
  - The system must have the ability to correlate healthcare patient identifiers with research identifiers for 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 subject information output.

- Additional data elements

- o In addition to structured domain data already collected in an EHR system, a minimum set of additional domain data needed for clinical research, as identified by CDISC CDASH Release 1 "highly recommended" elements, are included for the following domains: Demographic, Medical History, Medication, Adverse Event (Problems), Physical Exam, Vital Signs

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

- Added privacy features:
  - o Additional features for de-identifying research-bound data such that privacy regulations are met
- Added security features:
  - o 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, restrict data viewing)

- Added audit trail features:
  - o Additional Audit trail capabilities (e.g. feature to maintain a synchronization of audit trail to master clock, and maintenance of audit trail record after its associated patient record has been deleted)

6. References

Cancer Biomedical Informatics Grid (caBIG)
https://cabig.nci.nih.gov/overview/

- The caBIG initiative, overseen by the National Cancer Institute Center for Biomedical Informatics and Information Technology (NCI-CBIIT), was conceived to address the needs of all constituencies in the cancer community—researchers, clinicians, patients—to share data and knowledge, simplify collaboration, speed research to get diagnostics and therapeutics from bench to bedside faster and more cost-effectively, and ultimately realize the potential of Personalized Medicine. caBIG™ also addresses a critical problem facing both basic and clinical researchers today—an explosion of data that requires new approaches for collection, management, and analysis. Although initially focused on cancer research and care, caBIG™ technology is widely applicable to other therapeutic areas.

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

Clinical Data Interchange Standards Consortium (CDISC)
www.cdisc.org
- CDISC eSDI (eSource Data Interchange) document (20-Nov-2006)
- CDISC CDASH project: (Clinical Data Acquisition Standards Harmonization). The project goal is to develop a set of 'content standards' (element name, definition, and related metadata) for a basic set of global data collection fields (also known as CRF, or Case Report Form, variables) that will support clinical research studies. The initial scope of the project will be the 'safety data domains' (i.e. Adverse Events, Prior and Concomitant

Medication, Demographics and Subject Characteristics, Medical History, etc.). Version 1.0 was released 1-Oct-08.
- o www.cdisc.org/standards/cdash/index.html
- o CDSIC CDASH (Clinical Data Acquisition Standards Harmonization) Version 1: available at http://www.cdisc.org/standards/cdash/index.html
- CDISC / HL7 BRIDG project: (Biomedical Research Integrated Domain Group) Model is a domain analysis model representing protocol-driven biomedical/clinical research. It was developed to provide an overarching model that could readily be understood by domain experts and would provide the basis for harmonization among standards within the clinical research domain and between biomedical/clinical research and healthcare.

eClinical Forum
PhRMA EDC/eSource Task Force
www.eClinicalForum.com
- The Future Vision of Electronic Health Records as a Source for Clinical Research (14 Sept 2006)

EHRCR (Electronic Health Records for Clinical Research) Project
www.ehrcr.org
- EHRCR User Requirements Document (January 2010)
- HL7 EHR Clinical Research Functional Profile Release 1 (January 2009)

European Institute for Health Records (EuroRec)
www.EuroRec.org
- The EUROREC Institute (EuroRec) is an independent not-for-profit organization, promoting in Europe the use of high quality Electronic Health Record systems (EHRs). One of its main missions is to support, as the European authorized certification body, EHRs certification development, testing and assessment by defining functional and other criteria.
- EUROREC Repository : http://www.eurorec.org/services/repository.cfm?actief=services

European Commission: Justice and Home Affairs: Data Protection
http://ec.europa.eu/justice_home/fsj/privacy/index_en.htm
- Directive 95/46/EC on the protection of individuals with regard to the processing of personal data to protect fundamental rights and freedoms, notably the right to privacy and on the free movement of such data.
- Directive 2002/58/EC of the European Parliament and of the Council of 12 July 2002 concerning the processing of personal data and the protection of privacy in the electronic communications sector (Directive on privacy and electronic communications)

Health Level Seven (HL7)
http://www.HL7.org
- HL7 Electronic Health Record System (EHR-S) Functional Model Release 1 (Feb 2007)
- http://www.hl7.org/documentcenter/public/pressreleases/20070221.pdf

HIPAA (Health Insurance Portability and Accountability Act)
http://www.hhs.gov/ocr/privacy/index.html
- US Health Information Privacy

HITSP (Health Information Technology Standards Panel)
www.hitsp.org
- "Interoperability Specifications" - documents that harmonize and recommend the technical standards necessary to assure the interoperability of electronic health records and help support the nationwide exchange of healthcare data.

ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceutics for Human Use)
- Guidance for Good Clinical Practice E6(R1), 10-June-1996
http://www.ich.org/LOB/media/MEDIA482.pdf

- Guidance for Industry: E6 Good Clinical Practice: Consolidated Guidance (ICH (International Conference on Harmonization), April 1996) http://www.fda.gov/cder/guidance/959fnl.pdf

International Standards Organization (ISO)
www.ISO.org
- ISO/TR 20514: Health informatics, Electronic health record, Definition, scope and context. 2005-10-17

US Food and Drug Administration (FDA)
www.FDA.gov
- Electronic Records, Electronic Signatures Final Rule (21 CFR Part 11, 20-Mar-1997) http://www.fda.gov/ora/compliance_ref/part11/FRs/background/pt11finr.pdf
- Guidance for Industry: Computerized Systems Used in Clinical Investigations (CSUCI Guidance, May 2007) http://www.fda.gov/cder/guidance/7359fnl.htm
- Guidance for Industry: E6 Good Clinical Practice: Consolidated Guidance (ICH (International Conference on Harmonization), April 1996) http://www.fda.gov/cder/guidance/959fnl.pdf

US Health and Human Services (HHS) National Institute of Health (NIH):
http://privacyruleandresearch.nih.gov/
- The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule is the first comprehensive US Federal protection for the privacy of personal health information. Research organizations and researchers may or may not be covered by the HIPAA Privacy Rule. This website provides information on the Privacy Rule for the research community.

7. EuroRec EHRCR Functional Profile

Clinical Research Requirement ID	Requirement Description	EuroRec ID	Fine Grained Statement
EHRCR-T0-DA.100	The system can capture a minimum set of Demographic and Patient Characteristics data.	GS001519.03	The system stores key identifying information for each EHR and at least name, first name, gender and date of birth.
		GS005437.01	The system stores health item attributes as discrete data elements.
		GS005442.01	The system documents for each data element the source.
		GS005443.01	Each health item is stored as a discrete element.
		GS005468.01	The system can provide the ability to define a patient characteristic query and capture the response.
EHRCR-T0-DA.110	The system can capture a minimum set of Adverse Event data.	GS001534.02	The system maintains the onset date of each health event associated with a patient.
		GS001589.04	The system enables to identify a health item as an adverse reaction to a medicinal product.
		GS002271.02	The system enables to assign a degree of severity to a health item.
		GS002650.01	The system enables the user to label any kind of health item as a health issue.
		GS004974.03	The system enables the user to enter an allergy to dietary or environmental triggers or allergens.
		GS005430.01	The system enables the user to enter intolerances to drugs as well as to dietary or environmental triggers or allergens.

Clinical Research Requirement ID	Requirement Description	EuroRec ID	Fine Grained Statement
EHRCR-T0-DA.110 (Cont)		GS005431.03	The system enables the user to enter adverse reactions to dietary or environmental triggers or allergens.
		GS005436.01	The system stores each health event as a unique discrete entry.
		GS005437.01	The system stores health item attributes as discrete data elements.
		GS005441.01	The system enables the user to enter an allergy to a medicinal product or allergen.
		GS005442.01	The system documents for each data element the source.
		GS005443.01	Each health item is stored as a discrete element.
		GS005470.02	The system can capture, display and report all adverse events associated with a patient.
		GS005471.01	The system provides the ability to capture whether an adverse event is related to an Investigational Product or Procedure.
		GS005472.02	The system provides the ability to capture the action taken with regard to an investigational product or procedure if an adverse event occured.
		GS005473.01	The system can provide the ability to capture the outcome of an adverse event.
EHRCR-T0-DA.120	The system can capture a minimum set of Patient History data.	GS001608.01	The system stores and presents patient history.
		GS005436.01	The system stores each health event as a unique discrete entry.
		GS005437.01	The system stores health item attributes as discrete data elements.
		GS005442.01	The system documents for each data element the source.

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		GS005443.01	Each health item is stored as a discrete element.
EHRCR-T0-DA.130	The system can capture a minimum set of Medication/Therapy data.	GS001549.04	The system enables to enter medication items.
		GS001555.01	Each medication item has a start date.
		GS001558.01	Each medication item can have an end date.
		GS005436.01	The system stores each health event as a unique discrete entry.
		GS005437.01	The system stores health item attributes as discrete data elements.
		GS005442.01	The system documents for each data element the source.
		GS005443.01	Each health item is stored as a discrete element.
EHRCR-T0-DA.140	The system can capture a minimum set of Physical Exam data.	GS002374.01	The system is able to label a health item as a result of a clinical examination.
		GS002872.01	The system is able to label a health item as an assessment result.
		GS005436.01	The system stores each health event as a unique discrete entry.
		GS005437.01	The system stores health item attributes as discrete data elements.
		GS005442.01	The system documents for each data element the source.
		GS005443.01	Each health item is stored as a discrete element.
		GS005478.02	The system captures physical examination findings grouped per body system.
EHRCR-T0-DA.150	The system can capture a minimum set of Vital Signs data.	GS001971.02	The system enables the user to enter patient vital signs as discrete data.

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EHRCR-T0-DA.150 (cont)		GS001972.01	The minimal set of vital signs includes blood pressure, heart rate, respiratory rate, height and weight.
		GS005436.01	The system stores each health event as a unique discrete entry.
		GS005437.01	The system stores health item attributes as discrete data elements.
		GS005442.01	The system documents for each data element the source.
		GS005443.01	Each health item is stored as a discrete element.
		GS005444.01	The system keeps the original units in which measurement data were collected.
EHRCR-T0-DA.160	The system can capture a minimum set of Common Identifier Variables and Common Timing Variables.	GS001517.01	The system stores more than one identifier for each EHR.
		GS001610.02	The system enables to document a patient contact.
		GS005448.01	The system captures for each patient contact date and time.
		GS005450.01	The system enables the user to precise the type of patient contact.
		GS005481.02	The system can allow for unique research identifiers such that the research study can be identified.
		GS005482.02	The system can capture and maintain the site identification number(s) as assigned by the Clinical Research Sponsor.
		GS005483.02	The system can allow for unique research subject identifier.
EHRCR-T0-IO.200	System has the ability to store and retrieve data items in a way	GS002265.01	Each health item is uniquely and persistently associated with an identified patient.

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	that is attributable to a patient.	GS002307.02	Each patient and his EHR is uniquely and persistently identified within the system.
EHRCR-T0-IO.210	System has the ability to produce a human-readable copy of data (which includes associated audit trails and translation of any coded data).	GS001909.02	The system generates hardcopy output of predefined part of an individual EHR.
		GS001910.02	The system generates hardcopy of the complete individual EHR.
EHRCR-T0-IO.220	Specified de-identified data can be extracted for clinical research.	GS001938.01	The system enables de-identification of some data when extracting data from the system.
		GS002170.01	The system enables to extract patient data from the EHR according to a clinical trial protocol and template.
EHRCR-T0-IO.230	The system presents an overview of all patient consents and/or authorizations.	GS001767.04	The system presents a chronological overview of consents and/or their withdrawal for specific clinical activities.
EHRCR-T0-DS.300	System has an audit trail to include recording date/time/author of any data creation, change, or deletion.	GS001538.01	Each version of a health item has a user responsible for the effective data entry identified.
		GS002183.02	The audit log contains create/edit/ deleted events.
		GS002188.01	Audit log records include date and time of recordable events.
		GS002190.01	An audit log record includes the type of event (creating, editing, viewing, printing or electronically transferring all or any part of the patient health record).
		GS002191.01	An audit log record includes the user identity associated with a recorded event.
EHRCR-T0-DS.310	System does not allow new audit trail information to over-write existing (previous) information.	GS002198.02	Audit logs cannot be changed after recording.

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EHRCR-T0-BR.400	There are sufficient system and/or process controls for backup and recovery procedures.	GS002236.03	The system enables to make a backup copy of the application data.
		GS002237.02	The system enables to make a backup copy of the security management data.
EHRCR-T0-BR.400 (cont)		GS002238.02	The system enables to make a backup copy of the audit logs.
		GS002239.02	The system enables to restore application data from a backup copy.
		GS002240.01	The system enables to restore audit logs from a backup copy.
		GS002241.01	The system enables to restore security management data from a backup copy.
EHRCR-T0-DS.450	System limits the number of log-in attempts and records unauthorized access log-in attempts.	GS002185.01	The system enables to log authentication failures.
		GS002203.01	The system allows a configurable number of grace logins.
		GS002205.01	After the number of grace logins, only an administrator can reset the login of the user.
EHRCR-T0-DS.460	System allows and enforces password or other access keys to be changed at established intervals.	GS002206.01	The system enables to reset or change a password.
		GS002215.01	The system enables to enforce the security policy statements relating to re-use of passwords.
		GS002216.01	Security Policies contain rules for password life cycles.
EHRCR-T0-DS.470	System feature to allow automatic logoff or other data lock (such as password protected screen saver) after a set period of time of inactivity.	GS002655.02	The system has a timeout function, terminating a session after a configurable period of inactivity.
		GS003793.01	The system requires users authentication after a screen has been locked.
		GS005451.02	The system has a timeout function, avoiding screen access and data entry after a configurable short period of inactivity.

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EHRCR-T0-DS.480	Controls exist to ensure system date and time are correct (e.g. system clock synchronizes to a date and time provided by international standard setting agency).	GS002195.01	The system enables UTC time import from time servers for audit purposes.
EHRCR-T0-DS.490	The system has the ability to create, maintain and apply the roles, access permissions and capabilities of each user that accesses the system, such that users have access only to those system features and functions to which they have been granted access.	GS001512.01	The system enables to link a role to a user.
		GS002175.02	The system enables the implementation of a privilege and access management policy.
		GS002176.01	The system enables administrators to manage privileges and access.
		GS002415.02	The system takes the access rights into account when granting access to health items, considering the role of the care provider towards the patient.
EHRCR-T0-DS.500	Controls exist such that the ability to change system date or time is limited to authorized personnel and such personnel is notified if a system date change is detected.	GS005452.01	The system detects system date or time changes and notifies authorised personnel.
		GS005453.01	Only authorised personnel can change system date and time.
EHRCR-T0-DS.510	System allows audit trail to utilize standard time-keeping method such that the local time can be derived.	GS002196.01	The system enables the use of UTC (ISO 8601-2000) for date and time notation.
EHRCR-T0-BR.550	Process and/or system controls must ensure data used for clinical research source data are retained for the legal period.	GS001944.01	The system supports retention periods enforced by regulatory or legal requirements.
		GS005454.01	The system retains inbound data or documents as originally received.
		GS005455.01	The system documents for each data element and/or document the method of data entry.

Clinical Research Requirement ID	*Requirement Description*	*EuroRec ID*	*Fine Grained Statement*
EHRCR-T0-DS.600	There are sufficient system and/or process controls to prevent or mitigate effects of viruses, worms, or other harmful software code.	GS002254.02	Software installation media and software updates are screened for viruses by the vendor before shipping.
		GS004495.01	The system has tools activated to screen on harmful software code.
EHRCR-T0-BR.650	There are sufficient process controls for the system covering Disaster Recovery Procedures / Contingency Planning.	GS005456.01	Process control and disaster recovery procedures are in place.
EHRCR-T0-DS.700	The site has documented procedures for controlling user process at the site (system security measures, how source data are obtained and managed, what electronic systems are used).	GS005457.01	The system has documented use and security measures at site level.
		GS005502.03	Procedures exist on how the site obtain and manage source data.
EHRCR-T0-BR.750	The site has documented procedures for maintaining a copy of the source data at another location other than the clinical site.	GS005458.01	The system has a maintained copy of its data stored at a different location.
EHRCR-T0-TR.800	There is 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.	GS005459.02	Users of the system have appropriate education, training and experience of the system.
		GS005460.02	Personnel maintaining the system has appropriate education, training and experience to perform their task.
		GS005461.02	Developers of the system has appropriate education, training and experience to perform their task.
EHRCR-T0-SV.850	There is a vendor process to demonstrate that development and modifications of the system and system documentation use	GS005462.02	The system demonstrates and documents data integrity when installing software upgrade.
		GS005463.01	The system demonstrates and documents data integrity when installing security patches.

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EHRCR-T0-SV.850 (cont)	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 system and/or documentation, such as software upgrades, security and performance patches, equipment or component replacement.	GS005464.01	The system demonstrates and documents data integrity when replacing equipment or application components.
		GS005465.01	The system provider demonstrates that development and modifications of the system are based on good software development lifecycle practices including documented system validation and change control.
EHRCR-T0-SV.860	There is an investigator site 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.	GS005507.03	There is a Site process to document data integrity when changes to the system are applied.
		GS005508.01	There is a process to demonstrate that any changes to the system are documented.
EHRCR-T0-IO.900	There is 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.	GS005466.02	The system enables to identify and to list all personnel who have access to clinical trial data.
EHRCR-T0-DS.950	Measures must be in place such that persons who create, modify, or delete patient data items cannot modify the audit trail or the system clock.	GS002197.01	Only authorized users can access audit log records.
		GS002198.02	Audit logs cannot be changed after recording.