Bridging the gap on eSource Conformance

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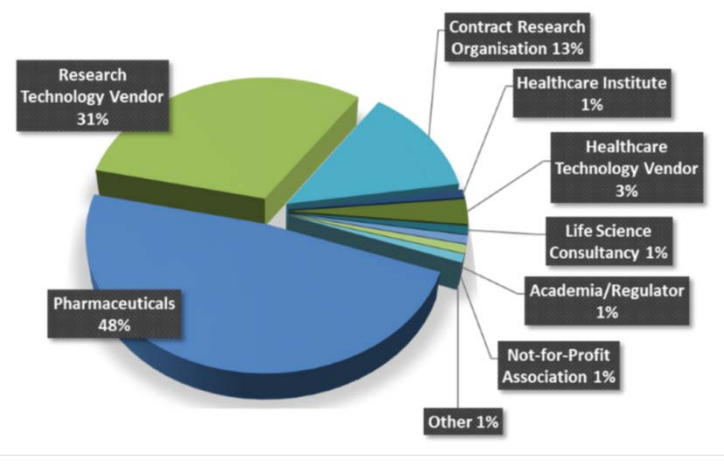
Highlights About the eClinical Forum

Multi-stakeholder input



US, EU and beyond

Continuing engagement

Preparing for public domain

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Content of the consultations with the EMA GCP IWG and the FDA eTeam

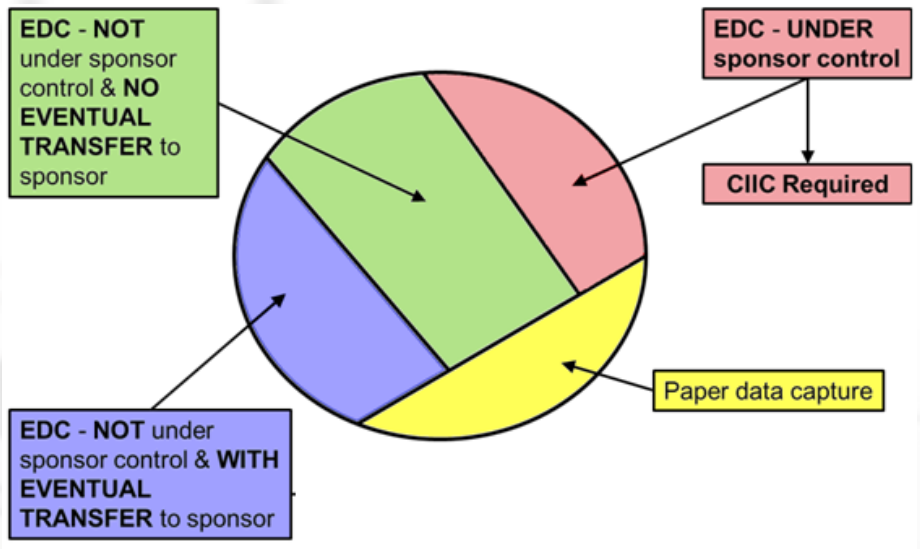
- Discuss the approach taken by the eCF EDC Hosting Task Force
- Identify and discuss diverging points of view related to the provided material
- The aim is to ensure patient safety, product quality and data integrity, recognizing that technology is not the only enabling factor

We are not seeking approval for documents or solutions – we are looking for an open & constructive dialogue

eCF EDC Hosting Task Force 2014 – increase scope in 2015

Concepts:

- Data Stewardship
- Clear segregation and documentation of roles and responsibilities for Sites and Sponsors
- eSource Checklist for assessment



Aim:

Best practice guide for a regulatory compliant EDC setup when using an independent third party (i3P), whereby the i3P assures that the Investigator retains control over his/her eCRF data

EDC Tasks and Activities – WP Section 5.

- EDC related tasks and activities were identified that are typically required during different phases of the study – for example eCRF design at study start; data entry, data review and querying activities during the execution phase of the study; and locking and archival activities at study closure.
- The scope of this part of the project was to develop detailed recommendations describing how these different tasks and activities should be performed and by whom, e.g. Sponsor/CRO, Investigator, EDC or i3p vendor.

Contracts and Agreements – WP Section 6.

- Focusing on the relevant Sections of ICH GCP - i.e. 4.9, 5.1 and 5.2 – as well as relevant parts of other pertinent information and guidance sources, for example Q&A sessions published by the EMA GCP IWG, as well as guidance documents and related supporting information published by the FDA, the relationships have been identified between the involved parties, and who delegates which tasks to whom – and, as a result, which contractual agreements and related tasks must be covered by the associated framework
- Active observers to the clarifications provided in the ICH E6 addenda. Documents will be reconciled.

Summary on EDC Tasks and Responsibilities (1/2)

WP	Task(s)	i3P	Site	Sponsor / CRO
5.1	**Account Management:**			
	- Application end users	If contracted	CONTRIBUTE	YES
	- Administrator privileged accounts	YES	NO	NO
5.2	EDC trial setup	If contracted	NO	YES
5.3	**Post-production Changes:**			
	- Investigator data not modified	If contracted	NO	RESTRICTED
	- Modifies Investigator data	RESTRICTED	ENDORSE	NO
5.4	Data Review and Cleaning	NO	CONTRIBUTE	YES
5.5	**External Data Load:**			
	- Load data copies	If contracted	NO	RESTRICTED
	- Directly transmitted data	YES	YES	NO

Summary on EDC Tasks and Responsibilities (2/2)

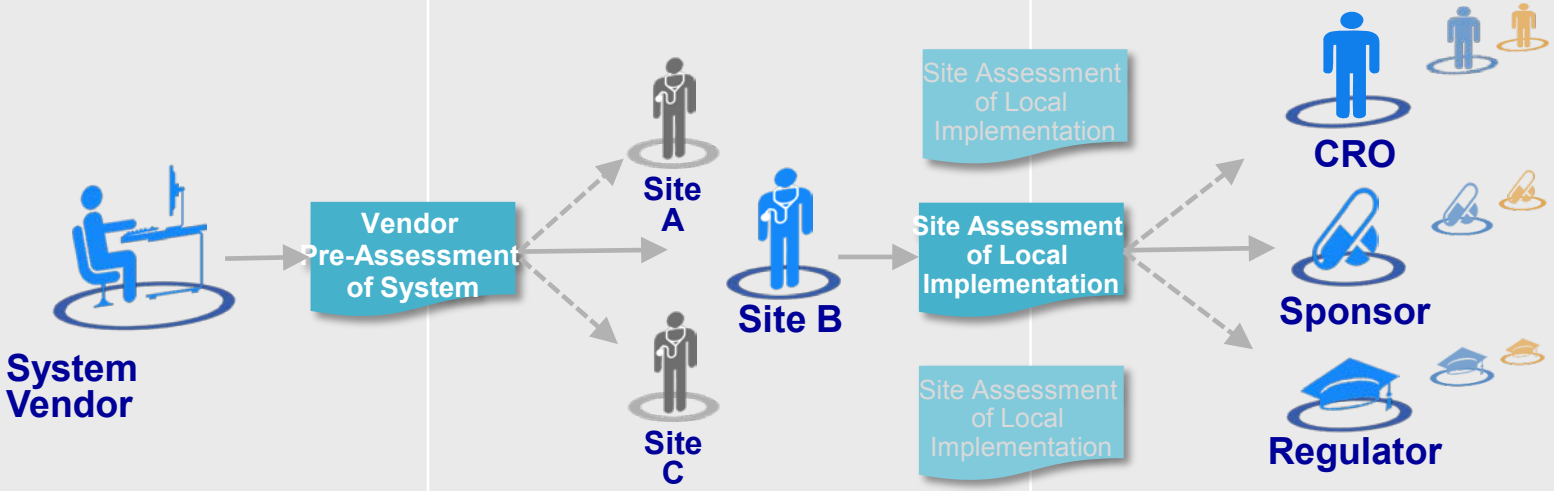
WP	Task(s)	i3P	Site	Sponsor / CRO
5.6	Data Extract	YES	RESTRICTED	YES
5.7	<u>Data Entry:</u>			
	- Investigator	NO	YES	NO
	- Other parties than the Investigator	NO	NO	RESTRICTED
5.8	Patient transfer	YES	RESTRICTED	RESTRICTED
5.9	Data changes outside the application interface	RESTRICTED	ENDORSE	NO
5.10	Locking / freezing of pages	If contracted	NO	YES
5.11	<u>Database Lock (Study closure):</u>			
	- Creation of ISDF file	YES	YES	INITIATE
	- Distribution of ISDF file	YES	ARCHIVE	RESTRICTED

eSource Checklist

- The eClinical Forum has in earlier projects (EHRCR and eSRA) defined in checklist form the criteria to be fulfilled in order for electronic source data from EHR systems to be acceptable for use in clinical research
- This work has been accepted internationally, and resulted directly in the HL7 EHR-S Functional Model specification and the EuroRec Functional profile for the reuse of EHR data for clinical research
- The criteria in the EHRCR checklist is applicable even to EDC systems (and other sources of electronic source data, such as ePRO systems)
- A number of requirements that were not applicable to EHR systems needed to be added (e.g. Sponsor control aspects)
- The resulting checklist can be used to assess any source of electronic data for compliance to inspector's expectations for clinical research

The eSRA Process

SYSTEM VENDOR *Completes Pre-Assessment*	CLINICAL RESEARCH SITE *Uses vendor Pre-Assessment to complete eSRA*	SPONSOR/CRO *Uses eSRA to work with site*
System Vendor completes eSRA Pre-Assessment as a resource for all their customers who run clinical trials	Site completes eSRA Assessment and provides to all their Clinical Research Sponsors	Monitoring staff use the Site eSRA and work with the site to achieve GCP compliance and to manage risk



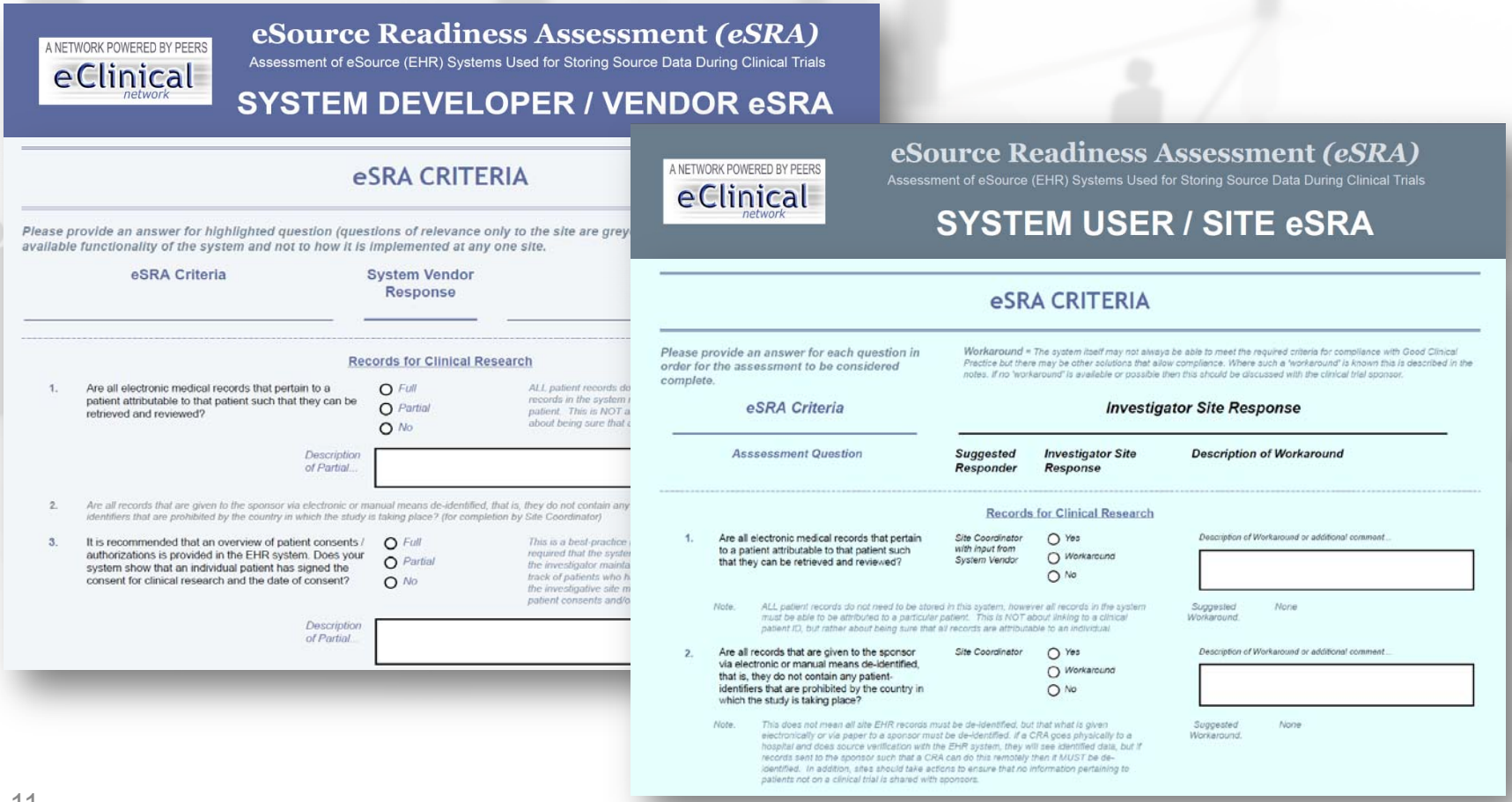
VENDOR: evaluate that your system has the required functionality... ONCE

SITE: use the vendor evaluation to check your operational system is compliant... ONCE

SPONSOR: use the system evaluation provided by the site instead of your own version

eSRA Assessment Templates

Global standards are maintained by the eClinical Forum to reflect the latest regulations, guidances and interpretations



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eSource Readiness Assessment *(eSRA)*

Assessment of eSource (EHR) Systems Used for Storing Source Data During Clinical Trials

SYSTEM DEVELOPER / VENDOR eSRA

eSRA CRITERIA

Please provide an answer for highlighted question (questions of relevance only to the site are grey) available functionality of the system and not to how it is implemented at any one site.

eSRA Criteria	System Vendor Response

Records for Clinical Research

1. Are all electronic medical records that pertain to a patient attributable to that patient such that they can be retrieved and reviewed? — ○ Full ○ Partial ○ No

Description of Partial...

2. Are all records that are given to the sponsor via electronic or manual means de-identified, that is, they do not contain any identifiers that are prohibited by the country in which the study is taking place? (for completion by Site Coordinator)

3. It is recommended that an overview of patient consents / authorizations is provided in the EHR system. Does your system show that an individual patient has signed the consent for clinical research and the date of consent? — ○ Full ○ Partial ○ No

Description of Partial...

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eSource Readiness Assessment *(eSRA)*

Assessment of eSource (EHR) Systems Used for Storing Source Data During Clinical Trials

SYSTEM USER / SITE eSRA

eSRA CRITERIA

Please provide an answer for each question in order for the assessment to be considered complete.

Workaround = The system itself may not always be able to meet the required criteria for compliance with Good Clinical Practice but there may be other solutions that allow compliance. Where such a 'workaround' is known this is described in the notes. If no 'workaround' is available or possible then this should be discussed with the clinical trial sponsor.

eSRA Criteria	Investigator Site Response		
Asssessment Question	Suggested Responder	Investigator Site Response	Description of Workaround

Records for Clinical Research

1. Are all electronic medical records that pertain to a patient attributable to that patient such that they can be retrieved and reviewed? — Site Coordinator with input from System Vendor — ○ Yes ○ Workaround ○ No — Description of Workaround or additional comment...

Note. ALL patient records do not need to be stored in this system, however all records in the system must be able to be attributed to a particular patient. This is NOT about linking to a clinical patient ID, but rather about being sure that all records are attributable to an individual.

Suggested Workaround. None

2. Are all records that are given to the sponsor via electronic or manual means de-identified, that is, they do not contain any patient-identifiers that are prohibited by the country in which the study is taking place? — Site Coordinator — ○ Yes ○ Workaround ○ No — Description of Workaround or additional comment...

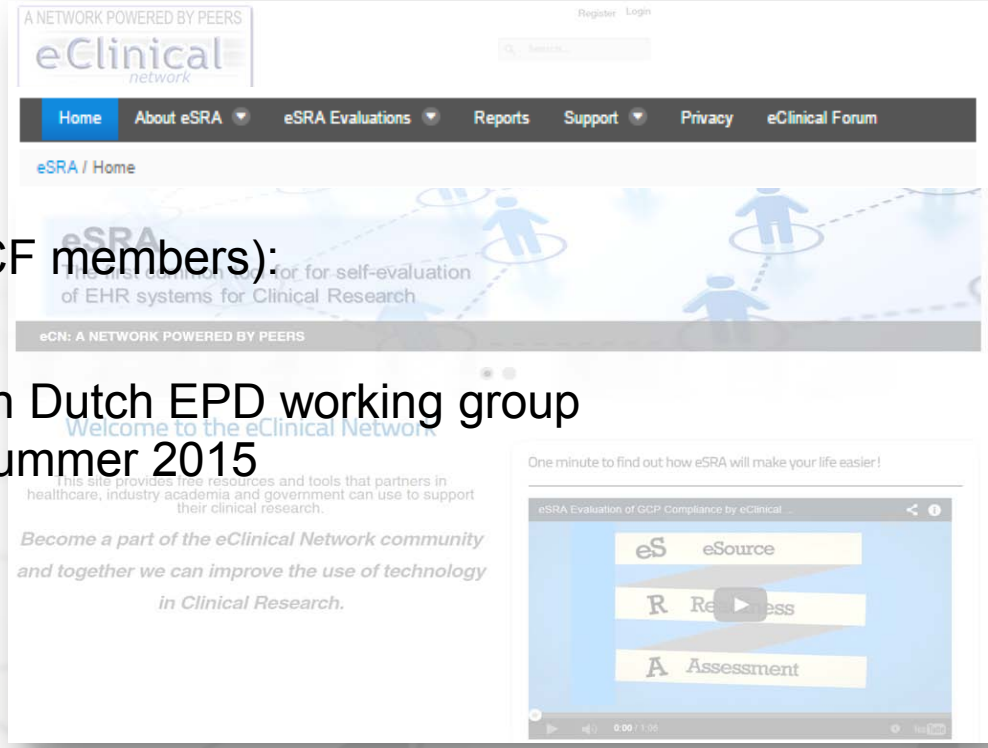
Note. This does not mean all site EHR records must be de-identified, but that what is given electronically or via paper to a sponsor must be de-identified. If a CRA goes physically to a hospital and does source verification with the EHR system, they will see identified data, but if records sent to the sponsor such that a CRA can do this remotely then it MUST be de-identified. In addition, sites should take actions to ensure that no information pertaining to patients not on a clinical trial is shared with sponsors.

Suggested Workaround. None

Integrated eSource requirements mapping proposal - Example

eSource Conformance Criteria (with EHRCR UR #s in parentheses)	MEETS ? Y=YES, N=No W=WORKAROUND	EDC/ePRO Sponsored Research systems	Independent eSource/EHRs (eSRA)
System has the ability to store and retrieve data items in a way that is attributable to a patient. (URC08)		x	x
Specified de-identified data can be extracted for clinical research. (URC10)			x
The system presents an overview of all patient consents and/or authorizations. (URC11)			x
System has an audit trail to include recording date/time/author of any data creation, change, or deletion. (URC12)		x	x
The audit trail includes the reason for changes /deletions.		x	x
The audit trail includes but is not limited to the following timestamps: • if not instantly available, the system shows when the record can be accessed by the Monitor or Data Management (Sponsor or Sponsor delegates) • PI Approval		x	
Audit trail/log information is readily available.		x	x

eSRA Update



- eSRA Release 1 (August 2015 for eCF members):
  - assessments completed off-line
  - pilot in December in partnership with Dutch EPD working group
  - volume testing completed in early summer 2015
- eSRA Release 2 in design phase :
  - online assessment
  - Looking for partners
- Possibility of adding other applications (e.g. EDC Assessment Checklist). **Integrated eSource Risk Assessment proposal**.
- Visit [http:\\eclinicalnetwork.org](http:\\eclinicalnetwork.org)

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Next Steps

- Maintain dialogue with EMA GCP IWG, FDA,. Bridge differences between QA stakeholders.
- Provide rationale and scope for the „right of inspection“ of shealthcare systems and processes
- Continue to collect further input / comments and distribute for formal review to:
  - Other groups, e.g. EFPIA, PhRMA, RQA,DM professional associations/SCDM
  - Additional key stakeholders, e.g. Investigational Sites
  - SDOs - CDISC
  - Other regulatory authorities i.e. PMDA,Chinese SFDA
- Refine White Paper and eSource Checklist accordingly
- Pilot eSource Checklist with Investigative Sites
- Release checklist to Sponsors, CROs and Regulators via the eClinical Network - done
- Publish final documents in 2015/2016 (dependent on E6 revision)