Electronic Data Capture —Selecting an EDC System

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1) Abstract

Electronic data capture (EDC) has become a preferred method for “real time” data capture in clinical trials. This chapter reviews the considerations for selecting an EDC system including evaluation of systems and vendors, user requirements, process change, and implementation of systems, so that the needs and requirements are identified to ensure a comprehensive study application. Multiple roles on study teams use the EDC system and should be involved in software selection.

After reading this chapter, the reader should understand

- The regulatory basis for practices in selecting an EDC system
- Common requirements and functionality domains of EDC systems
- Key domains and criteria for pre-selection evaluation of EDC systems
- Process impact and redesign considerations at evaluation and selection time
- Initial system implementation within an organization

2) Introduction

Historically, data for clinical trials have been manually abstracted from medical records, electronically extracted from medical records, or collected directly on Case Report Forms. (Collen 1990) For multicenter clinical studies a variety of approaches have been reported and an evolution toward decentralized entry of data is evident. Advantages of relocating data entry closer to the data source with data checks that flag discrepant data on the user interface during entry have been well articulated. (Kush 2003, Sahoo 2003, Schmidt 2005) Barriers and
challenges have also been enumerated and have evolved over time. (Kush 2003, Sahoo 2003, Helms 2001, Welker 2007)


Choosing an EDC system can and should be a significant decision for an organization. EDC system selection decisions are complex. Such decisions involve choices about processes for collecting and managing data that involve the entire trial team. Adopting new information technology offers new opportunity for process redesign such as workflow automation and other decision support. (Kush 2003) Organizations must decide to what extent a new system needs to support existing processes for data collection, management, and monitoring versus offer new ways of working. EDC system selection and implementation usually involves many stakeholders, including, but not limited to project management, data management, clinical management, biostatistics, and information technology.

While sometimes EDC systems are chosen for an individual study, more frequently, the chosen system will be used for multiple studies conducted by an organization and will impact operating procedures at clinical investigational sites and throughout clinical study operations. As the primary system for data collection and management in clinical studies today, EDC systems are a cornerstone, integral component of and leaping-off point toward future advances and ultimately greater safety, quality, and efficiency in clinical studies.

3) Scope

This first of three chapters on web-based Electronic Data Capture (hereafter EDC) covers considerations in and criteria and processes for selection of software for web-based EDC in clinical studies. Topics covered include common EDC system functionality, evaluation of candidate systems and vendors, and consideration of process impact and potential for process redesign at the time of system selection. The primary focus in this chapter is the identification of requirements for the EDC platform that are important to human subject protection and data integrity, including needs of system users and functionality necessary for Title 21 Part 11 compliance. Other important aspects of choosing an EDC system such as software delivery, acquisition models, and cost estimation are also addressed as is initial software implementation considerations.
Recommendations for building a study within an EDC system, testing a built study, study start-up, and provisions for change control for an EDC study are covered in the second EDC Chapter titled “Electronic Data Capture – Implementation and Study Start-up”. Aspects of study conduct and study closeout are addressed in the third and final EDC Chapter entitled “Electronic Data Capture – Study Conduct, Maintenance, and Closeout”. Good clinical data management practices apply to all types and sources of data. The EDC chapters contain applications of good clinical data management practices specific to data collection and management using web-based EDC. General good clinical data management practices are not re-articulated here.

4) Minimum Standards

The International Council for Harmonisation (ICH) E6 addendum contains several passages particularly relevant to EDC software selection and initial implementation. Section 2.8 states that “Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective tasks.” Echoing similar statements elsewhere in ICH GCP and in Title 21 CFR Part 11, this requirement applies to EDC software selection in that it applies to tasks in EDC system selection, installation, testing, use and maintenance whether they are performed in-house or elsewhere. Where tasks are performed by other organizations, this requirement is met through vendor qualification assessments, usually part of software selection decision-making. Where tasks are performed internally, costs for training and documentation of training are incurred.

Section 2.10 states that “All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification.” Functionality to meet this requirement becomes criteria used in software evaluation and selection.

Section 2.11 states that “The confidentiality of records that could identify subjects should be protected.” Functionality to meet this requirement becomes criteria used in software evaluation and selection.

Section 4.9.0 states that “The investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site’s trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).” This investigator site requirement applies to EDC systems because the EDC system can serve as the original capture of information, in which case, the EDC system is maintaining source data. Functionality to meet this requirement becomes criteria used in software evaluation and selection.

Section 4.9.2 states that “Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.” Functionality in EDC systems for triggering data to be source document-verified and tracking such verification supports this GCP requirement and become criteria used in software evaluation and selection.
Section 5.0 in the following passage recommends use of quality management systems and advocates risk management.

“The sponsor should implement a system to manage quality throughout all stages of the trial process.

Sponsors should focus on trial activities essential to ensuring human subject protection and the reliability of trial results. Quality management includes the design of efficient clinical trial protocols, tools, and procedures for data collection and processing, as well as the collection of information that is essential to decision making.

The methods used to assure and control the quality of the trial should be proportionate to the risks inherent in the trial and the importance of the information collected. The sponsor should ensure that all aspects of the trial are operationally feasible and should avoid unnecessary complexity, procedures, and data collection. Protocols, case report forms (CRFs), and other operational documents should be clear, concise, and consistent.

The quality management system should use a risk-based approach.”

A Quality Management System necessitates that executive leadership articulate and support a quality policy that documents leadership intent with respect to quality management. Because methods used to collect and manage data impact quality, executive leadership support for EDC selection and use is imperative. Further, leadership should assure that the quality management system extends throughout the organization and to vendors, suppliers, and sub-contractors where appropriate through a vendor qualification and management program.

Section 5.0.1 further advocates a process-oriented quality management system approach stating that “During protocol development the Sponsor should identify processes and data that are critical to ensure human subject protection and the reliability of trial results.” Processes reliant upon EDC software meet this requirement. EDC functionality to indicate and report separately receipt and status of data elements deemed critical is supportive of meeting this requirement and become criteria used in software evaluation and selection.

Section 5.1.1 further states that “The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirement(s).” Title 21 CFR Part 11 also requires SOPs for data collection, entry, and changes; in the case of EDC, these apply directly to clinical investigational sites as well as data sponsors. This functionality becomes criteria used in software evaluation and selection.

Section 5.1.2 protects access to source data and documents; “The sponsor is responsible for securing agreement from all involved parties to ensure direct access (see section 1.21) to all trial-related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by domestic and foreign regulatory authorities.” Where
the EDC system is used to collect and maintain source data, this criterion applies. EDC software functionality to support controlled and direct access to source data and documents supports this requirement and becomes criteria used in software evaluation and selection.

Section 5.1.3 states that “Quality control should be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly.” EDC system functionality to support automated detection, alerting, and tracking resolution of discrepant data directly supports this requirement as does functionality to support source document verification and reconciliation of data captured through EDC with externally collected or managed data. This functionality becomes criteria used in software evaluation and selection.

Section 5.5.1 refers to qualifications of study personnel and states that “The sponsor should utilize appropriately qualified individuals to supervise the overall conduct of the trial, to handle the data, to verify the data, to conduct the statistical analyses, and to prepare the trial reports.” This general requirement applicable to all data requires that personnel qualifications, including site users of EDC systems, with respect to the EDC software and its use be documented. The role of personnel qualifications in software selection decisions is described above with ICH E6R2 section 2.8.

Section 5.5.3 concerns validation of computerized systems and states that “When using electronic trial data handling and/or remote electronic trial data systems, the sponsor should, a) Ensure and document that the electronic data processing system(s) conforms to the sponsor's established requirements for completeness, accuracy, reliability, and consistent intended performance (i.e., validation).” This requirement echoes Title 21 CRF part 11 and requires that the installation of the EDC system used for a study be validated.

Section 5.5.3’s first addendum states that validation of computer systems should be risk-based. “The sponsor should base their approach to validation of such systems on a risk assessment that takes into consideration the intended use of the system and the potential of the system to affect human subject protection and reliability of trial results.” This general GCP requirement promotes right-sizing the type and extent of validation to the risk. In EDC systems, building a study within validated software has significantly less risk than developing new software. Open source software has different risks than commercial software or in-house custom-developed software. These risk differences are considerations in EDC software selection and initial implementation.

Section 5.5.3 addendum b states that an organization “Maintains SOPs for using these systems.” The 5.5.3 addendum c-h introductory statement enumerates topics that should be covered in SOPs. “The SOPs should cover system setup, installation, and use. The SOPs should describe system validation and functionality testing, data collection and handling, system maintenance, system security measures, change control, data backup, recovery, contingency planning, and decommissioning.” These requirements apply to system selection and initial implementation in that the processes covered by the requirement can be significantly impacted by the functionality available in an EDC system being used by a sponsor. Further, individual requirements in the section such as 5.5.3 addendum (e) “Maintain a list of the individuals who
are authorized to make data changes”, (g) “Safeguard the blinding, if any”, and (h) “Ensure the integrity of the data, including any data that describe the context, content, and structure”

e numerate functionality that become evaluation criteria to the extent EDC system support of these requirements is required by the organization.

Section 5.5.4 concerns traceability and states that “If data are transformed during processing, it should always be possible to compare the original data and observations with the processed data.” This requirement directly states functionality needed in EDC systems for GCP compliance.

Section 8.0 states that documents that “individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced” are considered essential documents (ICH E6) and shall be maintained as controlled documents. This requirement impacts EDC software selection and implementation in that EDC functionality to manage and control data specifications, including definition and specifications for programmatic operations performed on data, eases the external document control burden.

Title 21 CFR Part 11 also identifies regulatory requirements for traceability, training and qualification of personnel, and validation of computer systems used in clinical trials.

Requirements in 21 CFR Part 11 Subpart B are stated as controls for closed systems (21 CFR Part 11 Sec. 11.10), controls for open systems (21 CFR Part 11 Sec. 11.30), signature manifestations (21 CFR Part 11 Sec. 11.50), and signature/record linking (21 CFR Part 11 Sec. 11.70).

Requirements for electronic signatures are stated in 21 CFR Part 11 Subpart C. The requirements in Title 21 CFR Part 11 directly impact EDC software selection and initial implementation. Where Part 11 compliance is required, the technical controls stipulated become software evaluation criterion. These same requirements also appear on the traceability matrix used in software validation. Where the EDC system needs to be Title 21 CFR Part 11 compliant, which in the United States includes all studies submitted to the FDA for regulatory review as well as many studies funded by the National Institutes of Health (NIH), the Part 11 technical controls become software selection criteria.

The March 2018 FDA Study Data Technical Conformance Guide Technical Specifications Document is incorporated by reference into the Guidance for Industry Providing Regulatory Submissions in Electronic Format – Standardized Study Data. The appendix of the Study Data Technical Conformance Guide states that “In addition to standardizing the data and metadata, it is important to capture and represent relationships (also called associations) between data elements in a standard way”. As such, documenting associations between data elements becomes an EDC software selection criterion.

The Medicines and Healthcare products Regulatory Agency (MHRA) ‘GXP’ Data Integrity Guidance and Definitions provides considerations and regulatory interpretation of requirements for data integrity, such as:

Section 5.1 “Systems and processes should be designed in a way that facilitates compliance with the principles of data integrity.” The FDA defines data integrity as, “completeness,
consistency, and accuracy of data”. (FDA Dec 2018) and goes on to state that “Complete, consistent, and accurate data should be attributable, legible, contemporaneously recorded, original or a true copy, and accurate (ALCOA).” (FDA Dec 2018) Section 6.4 of the MHRA guidance similarly defines data integrity as, “the degree to which data are complete, consistent, accurate, trustworthy, reliable and that these characteristics of the data are maintained throughout the data life cycle. The data should be collected and maintained in a secure manner, so that they are attributable, legible, contemporaneously recorded, original (or a true copy) and accurate”. (MHRA 2018) Functionality to assure data integrity becomes EDC software evaluation criteria.

Section 6.9 of the MHRA guidance states, “There should be adequate traceability of any user-defined parameters used within data processing activities to the raw data, including attribution to who performed the activity.” (MHRA 2018) Functionality to assure data traceability becomes EDC software evaluation criteria.

The General Principles of Software Validation; Final Guidance for Industry and FDA Staff (2002) points out relevant guidelines regarding proper documentation expected of software utilized in a clinical trial. This guidance discusses software validation processes rather than functionality; these are not enumerated here. For commercial systems, this criterion can be met through a quality Management System assessment during vendor assessment. For in-house developed EDC software, this criterion is met through an internal Quality Management System that covers the software development lifecycle.

Good Manufacturing Practice Medicinal Products for Human and Veterinary Use (Volume 4, Annex 11): Computerised Systems (2011) provides the following guidelines when using computerized systems in clinical trials:

Section 1.0 echoes ICH E6(R2) stating that “Risk management should be applied throughout the lifecycle of the computerised system taking into account patient safety, data integrity and product quality. As part of a risk management system, decisions on the extent of validation and data integrity controls should be based on a justified and documented risk assessment of the computerised system.” This impacts EDC system implementation in the level of testing and controls applied and implies that a documented risk assessment exists for the system.

Section 4.2 “Validation documentation should include change control records (if applicable) and reports on any deviations observed during the validation process.”

Section 4.5 “The regulated user should take all reasonable steps, to ensure that the system has been developed in accordance with an appropriate quality management system.” For commercial systems, this criterion can be met through a quality Management System assessment during vendor assessment. For in-house developed EDC software, this criterion is met through an internal Quality Management System that covers the software development lifecycle.
Section 7.1 “Data should be secured by both physical and electronic means against damage. Stored data should be checked for accessibility, readability and accuracy. Access to data should be ensured throughout the retention period.” The technical controls for data access become software selection criteria. Readability, accuracy and other data quality dimensions may be impacted by incorrect system operation. Thus, validation testing should include assessing the data quality dimensions important to the Sponsor to assure that the system does not introduce errors.

Section 7.2 “Regular back-ups of all relevant data should be done. Integrity and accuracy of backup data and the ability to restore the data should be checked during validation and monitored periodically.” These become software selection criteria.

Section 10.0 “Any changes to a computerised system including system configurations should only be made in a controlled manner in accordance with a defined procedure.” For commercial systems, this criterion can be met through a quality Management System assessment during vendor assessment. For in-house developed EDC software, this criterion is met through an internal Quality Management System that covers the software development lifecycle.

GAMP 5: A Risk-based Approach to Compliant GxP Computerized Systems (2008) suggests scaling activities related to computerized systems with a focus on patient safety, product quality and data integrity. GAMP® 5 provides guidance for maintaining compliant computerized systems fit for intended use. While GAMP® 5 does not articulate additional functional requirements that impact EDC software selection, the evaluation of vendors, open source products, and development and evaluation of in-house software can all be informed by the approaches in GAMP® 5. GAMP® 5 provides the following guidelines relevant to systems used to collect and process clinical trial data:

Section 2.1.1 states that “Efforts to ensure fitness for intended use should focus on those aspects that are critical to patient safety, product quality, and data integrity. These critical aspects should be identified, specified, and verified.”

Section 4.2 “The rigor of traceability activities and the extent of documentation should be based on risk, complexity, and novelty; for example, a non-configured product may require traceability only between requirements and testing.”

Section 4.2 “The documentation or process used to achieve traceability should be documented and approved during the planning stage, and should be an integrated part of the complete life cycle.”

Section 4.3.4.1 “Change management is a critical activity that is fundamental to maintaining the compliant status of systems and processes. All changes that are proposed during the operational phase of a computerized system, whether related to software (including middleware), hardware, infrastructure, or use of the system, should be subject to a formal change control process (see Appendix 07 for guidance on replacements). This process should ensure that proposed changes are appropriately reviewed to assess impact and risk of
implementing the change. The process should ensure that changes are suitably evaluated, authorized, documented, tested, and approved before implementation, and subsequently closed.”

Section 4.3.6.1 “Processes and procedures should be established to ensure that backup copies of software, records, and data are made, maintained, and retained for a defined period within safe and secure areas.”

Section 4.3.6.2 “Critical business processes and systems supporting these processes should be identified and the risks to each assessed. Plans should be established and exercised to ensure the timely and effective resumption of these critical business processes and systems.”

Section 5.3.1.1 “The initial risk assessment should include a decision on whether the system is GxP regulated (i.e., a GxP assessment). If so, the specific regulations should be listed, and to which parts of the system they are applicable. For similar systems, and to avoid unnecessary work, it may be appropriate to base the GxP assessment on the results of a previous assessment, provided the regulated company has an appropriate established procedure.”

Section 5.3.1.2 “The initial risk assessment should determine the overall impact that the computerized system may have on patient safety, product quality, and data integrity due to its role within the business processes. This should take into account both the complexity of the process, and the complexity, novelty, and use of the system.”

The FDA guidance, Use of Electronic Health Record Data in Clinical Investigations, emphasizes that data sources should be documented and that source data and documents be retained in compliance with 21 CFR 312.62(c) and 812.140(d). It further states that “FDA’s acceptance of data from clinical investigations for decision-making purposes depends on FDA’s ability to verify the quality and integrity of the data during FDA inspections.” (FDA July 2018)

Section IV defines interoperability as, “the ability of two or more products, technologies, or systems to exchange information and to use the information that has been exchanged without special effort on the part of the user” and recognizes that “EHR and EDC systems may be non-interoperable, interoperable, or fully integrated, depending on supportive technologies and standards.” Where integration or interoperability is desired by the sponsor, these become EDC software selection requirements. Such requirements may include system support for data interchange according to specific standards such as the Health Level Seven Fast Healthcare Interoperability Resource (FHIR) standards or the CDISC Operational Data Model Standard (ODM).

Section IV.C states that “FDA encourages sponsors to periodically check a subset of the extracted [from EHRs] data for accuracy, consistency, and completeness with the EHR source data and make appropriate changes to the interoperable system when problems with the automated data transfer are identified.” Functionality in EDC systems accepting electronic EHR data to enter re-abstracted data and itemize discrepancies would support this guidance.
Section V.C.1 echoes the eSource guidance and states that the EDC system should have the ability to identify the EHR as “the data originator for EHR data elements gathered during the course of a clinical investigation”. (FDA July 2018) Where EHR interoperability is desired, this functionality becomes an EDC software selection criterion.

Section V.C.2 echoes the eSource guidance and states that “After data are transmitted to the eCRF, the clinical investigator or delegated study personnel should be the only individuals authorized to make modifications or corrections to the data.” (FDA July 2018) The section further states that “Modified and corrected data elements should have data element identifiers that reflect the date, time, data originator, and the reason for the change” and that “Modified and corrected data should not obscure previous entries”. (FDA July 2018) The same section further states that “Clinical investigators should review and electronically sign the completed eCRF for each study participant before data are archived or submitted to FDA”, that “If modifications are made to the eCRF after the clinical investigator has already signed the eCRF, the changes should be reviewed and approved by the clinical investigator”, and that use of electronic signatures for records subject to Title 21 CFR part 11 must comply with that regulation. (FDA July 2018) Where EHR interoperability is desired, this functionality becomes an EDC software selection criterion.

Further echoing the eSource guidance Section V.C.2 states that “If a potential for unblinding is identified, sponsors should determine whether the use of interoperable systems is appropriate or whether other appropriate controls should be in place to prevent unblinding.” (FDA July 2018) Where EHR interoperability is desired, this functionality becomes an EDC software selection criterion.

Similarly, the FDA’s Guidance on Electronic Source Data Used in Clinical Investigations provides guidance on the capture, review, and retention of electronic source data in FDA-regulated clinical investigations. The guidance “promotes capturing source data in electronic form, and it is intended to assist in ensuring the reliability, quality, integrity, and traceability of data from electronic source to electronic regulatory submission”. (FDA Sept 2013)

In the background section, the guidance states that “Source data should be attributable, legible, contemporaneous, original, and accurate (ALCOA) and must meet the regulatory requirements for recordkeeping.” (FDA Sept 2013) Record keeping requirements for clinical investigators and sponsors are detailed in Title 21 CFR 312.50, 312.58, 312.62, and 312.68 for drugs and biologics and Title 21 CFR 812.140 and 812.145 for medical devices.

Section III.A.1 states that all data sources (called originators in the guidance) at each site be identified. “A list of all authorized data originators (i.e., persons, systems, devices, and instruments) should be developed and maintained by the sponsor and made available at each clinical site.” (FDA Sept 2013) The guidance states that each data element is associated with a data originator. It goes on to state that “When a system, device, or instrument automatically
populates a data element field in the eCRF, a data element identifier should be created that automatically identifies the particular system, device, or instrument (e.g., name and type) as the originator of the data element.” (FDA Sept 2013) It is not clear whether the guidance recommends maintaining this association at the data value or data element level. However for a Title 21 CFR Part 11 audit trail, the association with the data originator and data changer is required at the data value level. Where the EDC system is the source, it should be on this list. In addition, EDC system functionality, where desired, for maintaining the data source list for each site, becomes a requirement in selection decisions.

Section III.A.1 of the guidance requires controls for system access and states that “When identification of data originators relies on identification (log-on) codes and unique passwords, controls must be employed to ensure the security and integrity of the authorized user names and passwords. When electronic thumbprints or other biometric identifiers are used in place of an electronic log-on/password, controls should be designed to ensure that they cannot be used by anyone other than their original owner.” (FDA Sept 2013)

Section III.A.2.d states that when data from an EHR are transmitted directly into the eCRF, i.e., electronically, the EHR is considered the source. The stated rationale is that algorithms are often needed to select the intended data value and that processing step necessitates verification. As such and where EHR-to-eCRF eSource data will be used, the ability to designate the EHR as the source for data values originating from the EHR becomes a requirement in EDC software selection.

Section III.A.3 states that “Data element identifiers should be attached to each data element as it is entered or transmitted by the originator into the eCRF” and that data element identifiers should contain, (1) Originators of the data element, (2) Date and time the data element was entered into the eCRF (this data receipt milestone is also time point at which the EDC system audit trail begins), and (3) association with the subject to which the data belongs. (FDA Sept 2013) The guidance further states that the EDC system “should include a functionality that enables FDA to reveal or access the identifiers related to each data element”. (FDA Sept 2013)

Section III.A.4 states that “Only a clinical investigator(s) or delegated clinical study staff should perform modifications or corrections to eCRF data”. (FDA Sept 2013) Echoing Title 21 CRF Part 11, the section goes on to state that “Modified and/or corrected data elements must have data element identifiers that reflect the date, time, originator and reason for the change, and must not obscure previous entries”, that “A field should be provided allowing originators to describe the reason for the change”, and that “Automatic transmissions should have traceability and controls via the audit trail to reflect the reason for the change.” (FDA Sept 2013) Where the EDC system is used to capture source data, these items become EDC software selection requirements.

Section III.A.5 states that the FDA encourages “use of electronic prompts, flags, and data quality checks in the eCRF to minimize errors and omissions during data entry”. (FDA Sept 2013) The rationale is that for eSource data, without an independent recording of the observation, the opportunity to make corrections to the source is gone after the time of the original observation
or measurement has passed. For this reason and where the EDC system is used as the original capture of source data, this becomes a requirement for EDC software selection.

The same section states that “clinical investigator(s) should have the ability to enter comments about issues associated with the data”. (FDA Sept 2013) Where the EDC system is used as the original capture of source data, this becomes a requirement for EDC software selection.

Section III.B.1.a states that to comply with the requirement in 21 CFR 312.62(b) for drugs and biologics and 812.140(a)(3) for devices to maintain accurate case histories, “clinical investigator(s) should review and electronically sign the completed eCRF for each subject before the data are archived or submitted to FDA” and that such electronic signatures must comply with Title 21 CFR Part 11. (FDA Sept 2013) This requirement applies more broadly than just where the EDC system is used as the original capture of source data and as such is routinely a requirement in EDC software selection.

Section III.B.1.b goes on to state that in the case where clinical investigators need to be blinded to certain data, the data are exempt from the aforementioned investigator review requirement. (FDA Sept 2013) Where the EDC system is used to capture eSource and blinding of investigators to data is intended, the functionality to do so becomes a requirement in EDC software selection.

Section III.B.2 anticipates the eventuality that data changes may be needed after a clinical investigator’s review and signature. The guidance states that in this case, “the changes should be reviewed and electronically signed by the clinical investigator(s)” (FDA Sept 2013) This requirement applies more broadly than just where the EDC system is used as the original capture of source data and as such is routinely a requirement in EDC software selection.

Section III.C states that “clinical investigator(s) should retain control of the records (i.e., completed and signed eCRF or certified copy of the eCRF) that “clinical investigator(s) should provide FDA inspectors with access to the records that serve as the electronic source data”, and that data and documents to corroborate source data captured in the EDC system may be requested during an inspection. (FDA Sept 2013) As such, where the EDC system is to be used as the original capture of source data, provision of a certified copy of all such data and relevant context such as the audit trail, data element identifiers, and data originators to the clinical investigator becomes a requirement in EDC software selection.

Section III.D emphasizes that the FDA encourages viewing of the data early and by sponsors, CROs, data safety monitoring boards, and other authorized personnel to prompt detection of study-related problems. The same section also suggests aspects of access control: (1) a list of the individuals with authorized access to the eCRF should be maintained, (2) only those individuals who have documented training and authorization should have access to the eCRF data, (3) Individuals with authorized access should be assigned their own identification (log-on) codes and passwords, and that (4) log-on access should be disabled if the individual discontinues involvement during the study. (FDA Sept 2013) These echo Title 21 CFR Part 11.
and apply more broadly than just where the EDC system is used as the original capture of
source data. As such these are common requirements in EDC software selection.

With these requirements in mind, we state the following minimum standards for the selection
and implementation of EDC systems.

- Secure upper management support for the selection of an EDC system and the
  functionality to be sought in the selection.
- Identify system requirements to be used as software selection criteria including but not
  limited to functionality needed for human subject protection, data integrity, and
  regulatory compliance.
- The identified functionality should be comprehensive for the organization and serve as
  the starting point of the traceability matrix used in software validation.
- If a commercial product is to be used, identify vendor selection criterion; these include
  functionality and quality management system components to be assessed as part of
  vendor qualification or other characteristics of the vendor.
- Perform and document a risk assessment with respect to the EDC system as intended to
  be used.
- Undertake and complete software validation activities and other controls
  commensurate with the risk.
- Assess and complete changes to Standard Operating Procedures (SOPs) and other
  governance policy and procedures necessitated by EDC-enabled processes.

5) Best Practices

- Identify the method of delivery required and ensure that internal or external skills are
  present to support the system and studies for which the system is used. [VI]
- Identify appropriate personnel participation in the investigation of EDC systems. [VI]
- Identify and leverage EDC functionality to improve data collection and management;
  e.g., provide decision support such as process automation and interoperability with
  other information systems. [III] (Kush 2003) (Wickens and Hollands 2016)
- Where software is acquired as a service or with services, prepare a thorough Scope of
  Work (SOW) to document and ensure complete understanding of expectations and
  deliverables. [III] (PMBOK 2017)

6) Stakeholders in the EDC System Selection Process

Choosing an EDC system involves multiple considerations including strategy, goals, business
relationships, and capability of the selecting organization and their desired provisioning models,
software functionality, system performance, and available funds. Thus, the list of stakeholders
in EDC selection and implementation can be extensive. Operationally, data collection and
management decisions such as whether EDC should be used and, if so, for which data and
through what types of processes can impact most operational groups involved in clinical trials.
Impacted operational groups include, but are not limited to, project management, data
management, clinical operations, research pharmacy, biostatistics, information technology, and
contracting. Individuals from all of these functional areas are possible stakeholders in the EDC
selection and implementation process. [VI] The likelihood that all stakeholder needs will be
reflected in the selection of an EDC system increases when those stakeholders and their
responsibilities are identified early in the decision making process. [VI]

7) EDC System Selection Considerations

There are over 60 EDC system vendors in the EDC market. (Capterra 2019) Companies enter
and leave the marketplace often. Though functionality is the most important category of
selection criteria with respect to data quality, other considerations such as regulatory
compliance, cost, vendor stability, business model compatibility, system flexibility,
implementation timing, and availability of support may narrow the number of appropriate
vendors. Kush et al. (2003) categorize EDC system selection criteria as aspects of vendor
background or product specifications. Product specifications are further categorized as
regulatory, standards, usability, operational and business. (Kush et al 2003)

a) Business and Financial

The cost of licensing an EDC system literally ranges from free to hundreds of thousands or
millions of dollars. Pricing models may vary among vendor organizations. Some charge by
data value, data element, or CRF screen while others charge by study or even
implementation. Other factors in pricing may include number of users and the services
provided by the vendor. In addition, consideration should be given to service level
agreements for availability of platform, system response time, and accessibility of support.
The purchasing organization may prefer making an upfront one-time investment versus
paying by study or incurring monthly fees. Organizational vendor contracting processes may
not allow for the type of service contract offered by the vendor. Organizational processes
may only authorize paying invoices for services that have been provided already, but a
vendor may require a quarterly payment upfront. For some organizations budget
constraints may be a large factor in a decision.

b) Timelines

The implementation timelines will also drive the selection process. The timing for the
installation and validation of the EDC system must be considered to ensure that the system
is ready to start a study build when needed and in full compliance with applicable
regulations. Additional timing considerations include training, length of time to build a study
specific application, and the extent of changes to organizational processes and SOPs
required.
c) Vendor Background and Stability

If the Vendor is a Public company, their financial and historical performance can be obtained freely. Knowing about the vendor is essential; questions such as these may provide insights:

- experience with the type or types of studies of interest
- experience in one or more therapeutic areas of interest
- experience in one or more regions of the world
- number of current/past customers
- software development experience
- aspects of the vendors software development quality management system
- number of employees
- ratio of development personnel to entire staff
- length of time in business
- financial stability
- past performance

Obtaining recent customer references is also strongly advised.

d) SOP compatibility

Current SOPs may dictate a specific process that the system may or may not support. For example, organizational SOPs may allow a Data Manager to review and close queries, regardless of how they were generated, whereas a system may only allow the “monitor” role to close queries generated during the source document verification process. Such a difference would require a work-around or change to organizational process. There are many opportunities for role-based functionality like that employed in most EDC systems to conflict with current organizational practices, roles, and workflow. These conflicts necessitate changes in organizational practices, generation of work-arounds, or changes in software functionality prior to implementation.

These organizational and business considerations may become selection criteria.

e) Software Functionality-based selection criteria

There is a core set of common EDC functions such as entering data and identifying data discrepancies covered by most EDC systems. However, vendors continue to use current and planned functionality to differentiate their system from other marketed systems. An initial step in selecting an EDC system is determining organizational functionality requirements. Some vendors attempt to cover a vast array of requirements through system configurability such as multiple options for handling workflow and data flow for diverse data streams. High levels of configurability may increase the complexity of setting up, maintaining, and migrating studies as well as software cost. How a necessary function is achieved within a system may be just as important as whether a system can accomplish it. Thus, in comparing overall cost, configuration should be included as well as the cost for achieving needed
features that are not covered by a system. In many cases a role-based workflow analysis, i.e., who does what and when, and data flow analysis will be helpful to determine configuration and implementation complexity and cost.

Common EDC product features are described but are not limited to those listed below.

**Support for a hybrid data entry model:** Some study scenarios include collection of data on paper. Several EDC systems now also have the capability of utilizing paper data entry into the same EDC database with eCRF data. These are called hybrid systems and allow for “Paper CRF” data entry (i.e., single or double data entry) by sponsor or designee personnel into the EDC system. Many EDC systems have the ability to set up two different types of form entry within the same build (i.e., single/double data entry (internal) and eCRF entry by site or other stakeholders) where entry rights are set by user permissions. Historically, the ability to enter data while not connected to the internet was offered with some systems. While not a large concern anymore in urban areas, offline capability may be important in remote regions of the world.

**Identification and resolution of data discrepancies:** Most EDC systems have the functionality to specify and execute missing and range checks during entry. Systems vary in the support for tracking discrepancies and their resolution, management of more complex checks, and management of checks against imported data.

**Medical Coding:** Medical coding features may include the ability to encode data during entry, facilitate encoding by a medical coder after entry, or facilitate exporting data for external coding. Some EDC systems include facilities for dictionary management and versioning.

**Safety Data Management:** Some organizations use separate safety data management systems and others manage the entire process out of the EDC system. Where an organization uses a separate system for Serious Adverse Event management, the ability of the EDC system to send information about AEs meeting the criterion of “serious” may offer efficiency and data quality gains. Where the EDC system is used to manage follow-up and reporting of SAEs, rule-based detection, notification, and workflow management for AEs and potential SAEs is often desired as is functionality to export populated MEDWATCH or CIOMS SAE-forms to Sponsor systems or for external reporting.

**Principle Investigator (PI) Signature functionality:** Some systems have methods to allow the PI to sign forms, visits, or casebooks in a controlled fashion. For example if data is changed after the PI has signed, the signature will be revoked.

**Importation of external data:** Study data often come from external organizations and devices such as laboratory data, Patient Reported Outcome (PRO/ePRO) data, and data collected from external devices. These data need to be imported and at minimum associated with the correct study subject and time point.
**Integration with other systems:** Real-time exchange and use of data is required for some studies. Some EDC systems include configurable application interfaces for the real-time exchange of data. Systems with which EDC systems interface may include clinical trial management systems (CTMS), randomization systems, systems at central labs, and PRO/ePRO systems.

**CTMS Integration:** Integration of the EDC system and the CTMS can be a powerful way to gain efficiency in the conduct of clinical trials. Specifically, the clinical data manager may want to integrate user account management. If site staff information is already being captured in the CTMS, this information may be transferred to either a help desk or directly into the EDC system, thereby eliminating manual creation of EDC accounts. Site status in the CTMS system, such as a site having clearance to enroll subjects, may be used as input into an algorithm to initiate access in the EDC system. Additionally, integration of visit information from the EDC system to the CTMS can facilitate monitoring and tracking of patient enrollment and completed patient visits. In turn, this information can be used to trigger site payments and grants. Integration of EDC with the CTMS also creates an ideal way to consolidate metrics used to assess overall trial performance.

**Randomization: IVRS/IWRS (IRT System) Integrations:** Randomization features may include randomization algorithms within the EDC system that automatically assign the treatment group, importing randomization lists, or interoperability with an external system used for randomization. Randomization functionality may support simple random sampling but may not support more complicated sampling strategies that include extensive blocking or balancing.

Interactive Voice Response Systems (IVRS) or Interactive Web Response Systems (IWRS) are often referred to as Interactive Response Technology (IRT) systems. Some EDC systems have built-in IRT system functionality that is fully integrated as part of the baseline configuration and other systems do not have this feature where integration from an external IRT system is necessary. In either case, the combination of this functionality integrated with the EDC provides a powerful solution that reduces data entry for site staff and ensures no transcription errors for this data across systems. Depending on which system is most convenient, the integration with EDC for sharing of information between databases is most important.

Integration of this data from external vendors involves building a secured pathway via a secure File Transfer Protocol (sFTP), Web Services (SOAP/REST), or other secure mechanism that will transfer the files generated from the vendor system and place these files in the EDC compatible host. This process is sometimes referred to as developing an IVR/IWRS program.

**ePRO Integration, Lab, CTMS, other:** If patient reported outcomes will be collected via the Web, an e-diary device, or other data device, clinical data managers should consider where and how this data will be integrated with eCRF data captured through the EDC.
If data collected using ePRO is needed for decision-making by the site, it may be worthwhile to upload ePRO data feeds into the EDC system. More ePro systems are now integrating data directly with EDC systems, as the efficiencies gained have helped reduce overall study costs.

**Laboratory Data Integration:** It is sometimes helpful to have all or key laboratory parameters available to site staff within the EDC system even if central laboratories are used. The clinical data manager should consider this need with the clinical team. Integrated laboratory data stored in a clinical database can facilitate more timely and robust edit checks across other eCRFs.

**Other External Data Integration:** If electrocardiogram, medical device, or other data are collected from external vendors, clinical data manager should evaluate whether data integration is appropriate. Again, integrations into an EDC system should only be performed if the data has direct impact on subject management.

**Clinical Data Management System (CDMS) Integration:** At some point in a study, data are integrated into one database. In some organizations this is done during a study to facilitate data cleaning and a Clinical Data Management System may be used. Unless a fully integrated EDC or clinical data management solution is used, clinical data managers should consider how an EDC system will integrate with new or existing clinical data management systems. The EDC vendor may be able to help with integration through an add-on component specifically designed to meet the system needs. Integration should encompass data and queries, while avoiding manual transcription of queries into the CDMS when automated edit checks occur in the EDC system. There should be careful considerations when evaluating CDMS integrations. Understanding baseline configuration and general form design differences will assist the clinical data manager with this decision.

Integrations should also consider the reporting needs for EDC data. Data from EDC, ePRO, an external vendor or other sources oftentimes need to be viewed together to assess data status, completeness, or payment milestones. A third party reporting tool or custom programming may be needed to achieve this. Where such data integration is not required for study operations, data from disparate sources may be merged via SAS prior to analysis.

**Electronic Health Records:** As the world is moving towards digitalization, the process of data collection is being transformed into electronic data sources, where the patient data is directly reported in the form of electronic source records. While building an EDC application it is important that consideration is given to the current and planned capability of the EDC system to receive data using healthcare-based exchange standards such as the Health Level Seven (HL7) Fast Healthcare Interoperability Resources (FHIR) standards. The system may be used purely for transfer of data from an Investigator controlled source to EDC. It is important that the EDC system be able to capture the information about the source from where the data is derived. (FDA EHR data use 2018)
**Other Important Integrations:** As new technological tools are developed, it is important to be mindful of other systems that may need to be integrated with an EDC system. In addition to the integrations discussed above, clinical data managers should be aware of the need to also integrate an EDC system with coding, and reporting tools other than SAS®.

**Different types of data:** Some data such as images or local labs bring additional requirements into consideration. For example local lab ranges are lab-specific, may change over the course of a trial, and are collected from each site. Images may require special processing and functionality to display.

**Services related to the data:** Some vendors or CROs offer data management services related to the study build, data management, and review of the study. If you are considering using services, these should be considered in the vendor selection process.

**Accessibility of data:** Data within the EDC system need to be accessible for analysis. EDC systems have facilities for exportation or accessibility of data. Data may be written out in different formats, such as SAS, xml, CSV. Vendors sometimes charge for each data transfer. Other systems offer self-service exports or direct access, e.g., read only views of the data. Other systems differentiate themselves by offering exports or views of study data in standard formats.

**Reports:** EDC systems often offer reports or report development and delivery functionality. Some systems offer standard operational reports, e.g., outstanding forms or queries, that cannot be customized for a specific study while other systems may offer varying degrees of report customization. Some systems offer facilities for visualization or ad hoc reporting of the clinical data.

**Tools for study building and writing data validation checks:** Some EDC systems include a graphical user interface for setting up eCRF screens and data validation checks while others require programming in various languages and to varying extents.

**Tools for documenting and managing user accounts:** Some systems track user training and have technical controls to enforce completion of training prior to system access while others do not. Other EDC systems additionally offer facilities for granting and revoking privileges and tracking these changes over time.

**Tools for managing risk based monitoring or partial Source Data Validation (SDV):** Some systems allow for and have features to help manage reduced SDV. Common features would include having the system identify a percentage of pages to be verified (to be set by the Data Manager) and having the system indicate critical variables that, for example, may require 100% SDV and are used for related reporting. The system should both support workflow for SDV and track SDV results.
Tools for multi-lingual forms: While data in many studies are collected in English across the globe, that is not always the case. Organizations may have a need for rendering study data collection forms in different languages and for maintaining synchronicity between form and rule versions across forms rendered in multiple languages.

Data export functionality: Getting data out of EDC systems is as important as getting it in. Functionality is usually needed to provide the site a pdf or other human readable enduring copy of the data entered from their site. In addition, functionality is required either from the EDC system or from a warehouse for authorized users to query the data directly. Situations often arise during a study that require ad hoc querying of the data to identify, confirm, or troubleshoot system or process problems. This functionality should always be available so that situations can be handled quickly when they arise. EDC system usually have functionality to provide customized and on-demand data exports in varying formats including CSV, SAS data sets, and xml including CDISC ODM. Many EDC system also support CDISC certified imports and exports of both data and metadata in bulk or “snapshot” or in transactional manner.

When considering features and functionality requirements, most vendors are in the continual process of improving/updating their system functionality. Therefore it may be important to understand features and their development timelines, such as whether the feature is a standard feature of the product in current release; a standard feature of the product in future release within the next 12 months; the feature needs a specific modification of the standard version, or the feature will not supported within the next 12 months. These are included in the sample Request for Proposals in the Appendix.

A good starting point for feature understanding is to think about needed system features in the context of a specific or typical project. The high-level business needs and desired system features form the requirements used in EDC system selection process.

Other specialized needs may include functions such as the following:

- Document Management such as providing a webpage for making current versions of study documents available to sites
- Integrating ePRO from hand-held devices or web surveys with CRF data capture
- Randomization
- Automatic reporting, sending out populated, e.g., CIOMS/AE-forms to external PV systems
- Generating or archiving PDF views for and from sites
- On Demand Export CSV, SAS programs and data sets, CDISC ODM
- Collection and management of reference ranges for local labs
- Multi-Lingual built in capability
- Collecting data for or triggering milestone base for Site Payments
- Supporting Offline Data Entry
- Offline
- Medical Coding by sites or essential coding
8) EDC Methods of Delivery

When considering the EDC system there are multiple options for delivery of the application. These include technical transfer, software as a service, and software as a service with services. The most used models today are software as a service and software as a service with services.

a) Sponsor/CRO purchases, installs and maintains the software

This is when an organization purchases a license to use software, acquires the software, and installs the software in an environment of their choosing. Requirements include having or having access to the appropriate hardware and network connectivity. Where Title 21 Part 11 compliance is required, the new installation has to be qualified, validated, and maintained under change control. There should also be procedures for the use and support of the system as well as training for system support staff. In this model, all study builds and upkeep are done in-house.

b) Software-as-a Service (SaaS) option

The SaaS option is sometimes referred to as hosting, or more recently as cloud computing and was formerly known as an Application Service Provider (ASP) model. Software as a service, e.g., provided via the internet, involves providing the hosted application as a service. The EDC vendor has all the software in their environment and it is accessed via the internet. A SaaS model may provide early benefits when starting out utilizing an EDC system. The EDC vendor can offer support and expertise for early trials based on previous experience. EDC trials may be initiated faster, since they are not dependent on a technical implementation. The pricing models differ between vendors; however, typically there will be the licensing fee to use the software, per study fees based on the time of trials, and per service costs. Study builds can be done by the sponsor or designee, e.g., a CRO or the EDC vendor.

c) SaaS with Services

Software as a service with services includes the vendor additionally providing services such as building the study application within the EDC system, training, or data management. Newer EDC applications that utilize cloud computing may offer “per-study” models. In this scenario the sponsor or designee pays for each study to be hosted. There will be a one-time upfront fee, the EDC vendor will build the study, there will be a monthly subscription charge to maintain and support the study, and there may not be a per user fee or per site fee.
d) Transition from one model to another

Where there is sufficient volume of studies, there is a natural progression for a SaaS with Services provider option to a SaaS model. After experience running studies with the system, an organization may gain capability and be comfortable performing study builds in-house rather than having the vendor provide that service. Similarly, an organization may gain experience and capability to maintain the software installation. These transitions offer potential cost reduction, increased convenience and control of eCRF build activities, increased access to integrated data, and opportunity for broader process optimization. Where these result in direct cost reduction or improved study conduct, maintaining study build capability internally may outweigh the associated cost.

Software and support services delivery models play a large part in setting roles and responsibilities between a vendor and customer. Determining and clearly articulating the roles and relationship(s) between the EDC vendor, sponsor, and CRO is a fundamental step in selecting an EDC vendor. This is particularly important in situations, where a sponsor uses multiple EDC systems with multiple models across multiple projects.

9) Business Requirements

As detailed in a sample RFP presented in the Appendix, business requirements can be categorized into high level concepts such as:
- General Information including Vendor, Product, and Support Information
- Contractual Information (licensing model, service, maintenance, and other agreement terms)
- Pricing Information
- Functional Requirements

As noted earlier, one of the key differentiating factors among different EDC systems is the functionality they provide. Hence, understanding exact business requirements and the associated functionality is imperative to choosing the right system. In the exploration of finding a system that best matches requirements, sponsors may find that more than one system will meet the needs of different studies they are planning. Perhaps a lower priced system will be adequate for the simple, short-term studies, whereas a higher end system may be best for a complicated long-term study. The appendix to this chapter provides a sample of how one company documented in detail their business requirements.

10) Selecting and Contracting

There are multiple activities associated with selecting and contracting an EDC vendor.
a) **Selecting an EDC System**

Specific project needs should be identified and a Request for Information (RFI) and/or Request for Proposal (RFP) should be sent to specific EDC vendors for consideration. An RFI is a document that an organization sends to prospective vendors to ask for specific information or clarification on services or products. Often the information obtained will be used to shorten the list of vendors or contractors from which proposals will be requested. A request for proposal, or RFP, is the document that an organization sends to prospective vendors to formally request a proposal and associated cost.

Both documents are normally used in the early stages of vendor selection, with the RFI typically sent earlier than the RFP. The proposals are often used as the basis for selecting the vendor outright or for creating a short-list of vendors from whom presentations will be requested. Often the vendors will have the opportunity to demonstrate the EDC functionality as well as the vendor capabilities. Key vendor personnel will be present and it is important to include key stakeholders in these presentations and to request demonstration of functionality required for your organization. Often organizations will rate proposals and functionality against a grid like that provided in the Appendix. Once all of the presentations have concluded, additional selection criteria may include past, ongoing or future projects within the program, vendor performance history, vendor experience with previous industry studies and references from current/former customers. See the Vendor Selection and Management Chapter of the GCDMP for more information on contracting models and processes.

b) **Contracting an EDC vendor**

The Statement of Work or Scope of Work (SOW) is often an attachment to the contract with a vendor. The SOW describes in detail the work to be performed, for example, implementation support or study set-up and execution, often with estimated timelines and milestones. The SOW is usually negotiated and the negotiations on the SOW or contract language may go for several rounds before the final version is signed by all parties. Upon finalization of the SOW, the Sponsor project team may choose to kick-off the project or relationship with a meeting between the EDC Vendor and Sponsor or CRO teams to introduce team members, review SOW highlights, discuss Vendor processes and templates, identify anticipated complexities and risks, and agree on the implementation timelines and a meeting schedule.

c) **Software Validation**

In the paper model, although there is significant work done ahead, it is realistic that data collection can begin once a paper CRF has been created. In EDC, the data collection method is much more than a piece of paper—it is an entire software application; therefore the entire scope of validation activities should be completed up-front. One of the biggest benefits of utilizing EDC is that the data are cleaned at entry and is available for review in real time.
When using an EDC application there are important considerations that the sponsor needs to consider regarding the validation of the chosen system. The EDC system and each application/study that is built using this system should adhere to a validation process. Code of Federal Regulations, Title 21, Part 11 and the US Food and Drug Administration Guidance for Industry: Computerized Systems Used in Clinical Trials specifically mention the validation of the program(s) to be used.

When choosing an EDC system or vendor, it is the responsibility of the Sponsor to ensure that the System has been developed and is maintained per an acceptable Software Development Life Cycle (SDLC) process. Where a hosted vended system is used, to ensure the vendor’s system meets the requirements, an in-person or virtual Audit is usually performed of the vendor SDLC documentation. Where software is installed locally, a vendor audit is usually conducted and is followed by installation. The validation process usually follows contract execution.

11) Recommended Standard Operating Procedures

- EDC system selection
- EDC System Setup, Installation and Support
- Software Development Lifecycle
- Vendor selection, auditing and oversight

12) References


13) Authoritative References (Regulation, Guidance and Standards)

1. U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Center for Biologics Evaluation and Research


6. GAMP® 5: A Risk-Based Approach to Compliant GxP Computerized Systems. 2008, ISPE, Tampa, FL.


8. United States Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER), CDER Data Standards Program. Available from the U.S. FDA at FDA Data Standards Catalog https://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm Accessed March 11, 2018


14) **Further Reading**

3. Brigitte Walther; Safayet Hossin; John Townend; Neil Abernethy; David Parker; David Jeffries. *Comparison of Electronic Data Capture (EDC) with the Standard Data Capture Method for Clinical Trial Data*. *PLOS ONE*. September 23, 2011. https://doi.org/10.1371/journal.pone.0025348
6. Ed Kellar, MS, Susan M. Bornstein, MPH, Aleny Caban, BS, Catherine Célingant, MA, Michelle Crouthamel, MS, Chrissy Johnson, MS, Patricia A. McIntire, BSc, Kenneth R. Milstead, MS, Jaclyn K. Patterson, BS, Brett Wilson, BSP, Optimizing the Use of Electronic Data Sources in Clinical Trials: The Landscape, Part 1. Therapeutic Innovation & Regulatory Science 2016, Vol. 50(6) 682-696https://doi.org/10.1177/2168479016670689
Appendix: Sample Request for Proposal (RFP)

Introduction

1.1 Scope

1.2 Objective

The main objective of this Request for Proposal (RFP) is to identify a software product suitable to design, build, and manage clinical trial databases utilizing Electronic Data Capture. This RFP is designed to select a flexible Electronic Data Capture (EDC) system that provides Sponsor CDM staff with strong backend Data Management capabilities. The product also serves to meet the following goals:

1. To harmonize Data Management processes
2. To centralize Data Management for all trials
3. To provide ease of system use for users
4. To continue to take ownership of database build and edit check programming activities
5. To provide tools for tracking project status and project details
6. To support metrics driven Data Management processes.

Vendor products will be evaluated with respect to the SPONSOR functional requirements mentioned in this RFP.

1.3 Calendar of Events

(RFP release date; anticipated timeline for any formal presentations or notifications, e.g., short list notification, and making a selection decision)

SPONSOR plans to review RFP responses during DATE RANGE. Vendors will be individually notified by SPONSOR after the review of responses to this RFP on or around DATE. If short-listed, sales and technical staff will be invited to demonstrate product capabilities on or around DATE. Demonstration requirements will be specified when potential vendors are notified of short-list selection to provide presentation for SPONSOR. We anticipate making a product selection by DATE.

1.4 Deadline for Responses

2 General Information

2.1 Vendor Information
Provide all information requested in the following sections. If available, attach documentation to support the information given.

2.1.1 General
a) Company Legal Name.
b) Doing Business As.
c) Main Headquarters Address.
d) Company Web Site.
e) Main Telephone Number.
f) Main Contact Person and Information for this RFP.
g) Year Founded.
h) Legal Form/Ownership.
i) Private/Public.
j) If Private, identify principle equity holders, including country of origin.
k) Division of (if a division of a larger legal entity).
l) Main Headquarters Address and Web Site of Parent Company (if any).
m) Number of Offices (total including affiliates).

n) Has the company ever been part of a merger or acquisition with another company?
o) Is the company currently part of a pending merger or acquisition with another company?
p) Partnerships with other companies.
q) Number of clients by type of client:
   • Pharma
   • Biotech
   • Medical Device – And provide % of business this comprises.
   • CRO – And provide % of business this comprises.
   • Other
r) Identify any services/products that are supplied by other partners/vendors.
s) Has the company discontinued any business lines in past 5 years? If yes, please describe.
t) The employee turnover history. Percentage of employee turnover rate for 20xx and 20xx.
u) Number of permanent employees as of this RFP.
v) Number of contract employees as of this RFP.
w) Expected total number of people employed at year-end 20xx.
x) Ratio or percentage of sales people to technical employees within the company.
y) Number of personnel (sales, technical, or other) who have professional background in clinical trial operations in former job venues.
z) Present or past bankruptcy procedures involving the vendor and/or parent company.
aa) Present or anticipated bankruptcy filing by the vendor and/or parent company.
bb) Litigation procedures involving the vendor and/or parent company.
cc) Annual Revenue.

2.1.2 Company History and Performance
a) The percentage of business directly related to the proposed product type.
b) The total number of EDC or CDMS systems installed to date similar to the proposed SPONSOR product.
c) The total number of clinical trial studies started and in “conduct” stage to date.
d) The total number of clinical studies concluded and archived to date.
e) The total number of clients to date.
f) Total number of clients currently being served in parallel.

2.1.3 Company Process and Procedure
a) Describe your Software Development Lifecycle Process.
b) Provide a table of contents of your Standard Operating Procedures.
c) Are your Standard Operating Procedures and System Validation documentation available for auditing? If so, what is the minimum lead-time needed to schedule an audit?
d) Have you ever been audited by a regulatory agency (i.e. FDA)? If so, when and was a report issued? Have you or any Sponsor studies for which your system was used received an FDA Form 483; If so, please list all instances and describe the findings and your corrective and preventative actions?

2.2 Product Information
2.2.1 Product Sales Information
a) The year the product was first packaged for market.
b) The product past release history.
c) The number of copies sold.
d) The number of copies sold during the last 12 months.
e) The last and next release dates.
f) The number of patches released over the last 12 months.
g) Studies developed, managed or hosted by your company including the number of existing studies.
h) References from the medical device and pharmaceutical/biotechnology and CRO industry sector. If available, include:
   - The company name, address and the contact person’s name, title and phone number.
   - A description of the environmental similarities between the company and SPONSOR

i) If a user group(s) exists, include for each user group type:
   - A description of meeting frequency and location, years in existence, membership fees, number of active members and the group coordinator’s name and phone number.

2.2.2 Support
a) Does your company provide technology transfer? If so, describe scenario of how your company would implement a full technology transfer with SPONSOR, including process, timelines, and cost.

b) Number of clients and % of business they comprise by type of client:
   - SaaS Model
   - Full tech transfer
   - Hybrid or “staged” (i.e. gradual tech transfer where client builds and deploys their own databases, but relies on your company (the vendor) to provide hosting and technical/ help desk support)

c) Examples of installations where worldwide Help Desk is currently provided or is being planned

d) Implementation and Validation: Typical time frame for system installation and installation validation. Include the number of FTEs required for both tasks.

e) Indicate the services provided by the vendor from the following list:
   - Package installation (IQ, OQ, PQ including validation scripts)
   - Implementation and Deployment Methodology
   - User Training
   - Operator / System Administrator training
   - User support

2.3 Additional Information
Provide the same information about sub-contractors, if sub-contractors are anticipated to play a significant role in the product implementation.

3 Contractual Information (License, Maintenance Agreements, etc.)
Provide all information requested in the following sections. If available, attach documentation to support the information given.

a) Standard License or Master Service Agreement
b) License limitations (e.g., right to copy, right to transfer, use by co-ventures, etc.).
c) Terms of license
d) Standard Maintenance Agreement
e) Optional support services.
f) Group agreements.
g) If existing software is customized for this project and SPONSOR is paying for customizations, describe the following:
   • Right of ownership.
   • The royalties, if the vendor intends to sell.
   • Standard contractual secrecy obligations.
h) Contract provision for penalty costs and time limit for formally reporting breach of contract if product fails to perform as per specifications
i) Escrow Agreement.
j) Policy regarding access to source code.

4 Pricing Information

SPONSOR will consider a variety of pricing models available. SPONSOR expects the following number of users to require user accounts for the product and for paper based trials. We anticipate using the system for NUMBER clinical studies of approximately NUMBER sites and NUMBER patients and each undergoing active enrollment, data collection and follow-up for a duration of NUMBER years.

1) X personnel from Clinical Data Management (CDM)
2) 2 Medical Coding Specialists (not included in the above CDMs)
3) 1 Biostatistician
4) 1 Data analyst

Describe each cost area in detail.
   a) Standard license or leasing (per usage level) costs.
   b) Standard maintenance costs.
c) Standard technical support costs.
d) Standard training costs.
e) Installation costs/validation costs.

SPONSOR is sensitive to costs, cash flow, and value of service. Pricing models that appeal to the flexibility that this niche demands will be given careful consideration in this vendor selection process.

5 Functional Requirements

The proposed solutions should cover applications in the areas of:

- Electronic Data Capture (EDC)

The vendor may describe additional features of the proposed products that could be of interest to SPONSOR under each heading or in separate documentation as appropriate.

5.1 CRF and Database Design

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<td>2. Standard feature of the product in future release within the next 12 months.</td>
</tr>
<tr>
<td>4. Not supported within the next 12 months.</td>
</tr>
</tbody>
</table>

Data entry screens capable of being programmed to resemble layout of paper CRF.

Ability to automatically generate annotated CRF.

Ability to automatically generate database structure documentation.

Web Collaboration tool for CRF design review.

Global CRF Standards library supporting three tiers (i.e., general standards, therapeutic area specific standards and trial specific data modules):
- Global Library supporting two flags for data elements: mandatory flag and optional flag.
- Global Library containing database structure, screen definition and edit check programs/rules

Flexible data entry screens can be designed by a novice user in Clinical Data Management.

Data entry screen sequence customizable to follow a logical decision tree.

Ability to use same tool for both EDC and Paper Trials.
5.2 Database Build
| 2. Standard feature of the product in further release within the next 12 months. |
| 4. Not supported within the next 12 months. |

**Support of different field level data entry conventions:**
- Mandatory “always” (e.g., Patient initials)
- Mandatory but with the possibility to leave it empty by clicking the related NA (not available or missing) check box; ability to enter NA in all fields including numeric and date fields
- Mandatory but with the possibility to leave it empty by introducing the related explanation

**Support of automatic conversion of values expressed in different units into standard units (e.g., inch$\rightarrow$cm).**

**Audit trail information at field level including:**
- User
- Date/Time of modification
- Old and new value of the amended field
- Reason for amendment

**Data fields are associated with a descriptive SAS label that can be defined and are retrievable by SAS programmers.**

**Ability to store both text and codes (e.g., YES/NO or 1/2).**

**Capability to generate data sets from a user friendly interface.**

**User friendly drag and drop, point and click based rules builder using a rules wizard.**

**Dynamic forms and visits.**

**Functionality to design output driven data sets in the context of the study build.**

**Repeating modules or variations of repeating modules can be applied to various unique CRFs for front end use, while data is related and stored on the backend in a single data set.**

**Data entry screens and views built in the architect/test module looks the same in both the architect/test module as it does in the production database.**

**A dataset (containing approximately 20 variables) takes no longer than 30-45 minutes to construct in study build.**

**Drag and drop, click and dragging entry screen objects preferable for programming (compared to non-intuitive interfaces requiring complex programming).**

**Ability to copy and modify databases or database objects from one study for use in another trial.**

The following data entry fields can be programmed:
- open text/character fields (up to 500 characters) with wrap-around capability
- numeric fields, date fields, time fields, drop down lists, check boxes, radio buttons

Data entry fields can be formatted (e.g. left/right/top/bottom alignment, wrap-around is minimized, excessive scrolling to the right or down can be minimized, etc.).

Ability to configure date fields to allow partial dates without front-end data checks firing.

Code lists can be employed so that codes associated with text values are easily retrievable by SAS programmers.

System allows for double data entry with arbitration for paper-based trials.

Data fields can be configured as either single pass or double pass. (CRFs, not individual fields)

Ability to indicate responses as 'Not Done' or 'Not Applicable' or 'Unknown'. These values should be contained within the back end dataset and not within a separate table so that edit checks may be run against them, etc…

Ability to enter data into a field if the data does not conform to all field requirements (e.g. a number is recorded in a text field on the CRF).

Ability to link Adverse Events and Medications for each patient.

Data exports are compliant with CDISC SDTM and ODM data models.

A separate test environment for validation and testing of both database and edit checks that is outside the production environment, either hosted on a separate server or a validation area built into the product that functions in the same manner as the production environment. Once validation and testing have been performed, the database and/or edit checks (as well as updates) can be released into the production environment.

CDASH standard eCRFs available out of the box with the software.

Ability to configure email alerts based on defined criteria.

<table>
<thead>
<tr>
<th>5.3 Edit Check Programming</th>
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</thead>
<tbody>
<tr>
<td>2. Standard feature of the product in further release within the next 12 months.</td>
</tr>
<tr>
<td>4. Not supported within the next 12 months.</td>
</tr>
</tbody>
</table>

Query text for edit check output can be defined upon programming edit checks.

Ability to add edit checks after the database is in production.
User friendly drag and drop, point and click based rules builder using a rules wizard.

Ability for query text to be configurable such that actual discrepant data values can be populated within query text automatically when check fires.

Query text length is at least 500 characters.

Groups of edit check programs may be run against trial data.

Ability to program the following types of checks:
- Within form checks,
- Cross form / cross data set checks

Edit check functionality can be applied to unscheduled visits / forms.

Batch validation can be initiated at any unscheduled time (e.g. manually).

Batch validation can be scheduled at pre-defined time points as needed to avoid system performance issues during peak usage times.

Edit checks can be configured to fire at point of initial data entry.

Visual prompts or dialogue boxes that pop up when non-conformant data is entered into a formatted data field.

System has a mechanism for capturing non-conformant data or forces the user to enter a conformant value.

Edit checks to be configured to fire at point of initial data entry or during batch validation or upon completion of second pass data entry arbitration.

Ability to program automated data checks involving a single data field can be configured within context of database build features or through programming apart from the build of the actual data fields.

Drag and drop, clicking and dragging data field objects into equations with operators (as opposed to non-intuitive interfaces and complex programming).

Ability to define univariate checks through database build set-up.

Fire during batch validation or when interdependent conditions are met as defined in the edit check programming specifications.

Ability to program automated data checks involving multiple data fields and multiple datasets that can be configured through programming or in an architect tool builder.

Ability to compare multiple data fields within the same CRF.

Ability to compare multiple data fields across different CRFs.
### 5.4 Database Amendments

1. **Standard feature of the product in current release.**
2. **Standard feature of the product in further release within the next 12 months.**
3. **Needs a specific modification of the standard version.**
4. **Not supported within the next 12 months.**

- Database amendments (CRFs and edit checks) and post production changes can be performed without disabling the database for an extended period of time.
- Amended structures can be done at the module level, tested in a validation area, and then released into the production environment.
- Design and testing in the validation area does not disrupt ongoing data processing in production.
- Database can be versioned at the module/data set level (as opposed to the CRF or page level).
- Database version is identifiable within the interface for applicable modules, forms or datasets.
- Ability to apply newly versioned CRFs to specified subjects while allowing former version(s) to remain in effect for other specified subjects to whom the amendment does not apply.

### 5.5 End-User Interface

1. **Standard feature of the product in current release.**
2. **Standard feature of the product in further release within the next 12 months.**
3. **Needs a specific modification of the standard version.**
4. **Not supported within the next 12 months.**

- Flexible application menu definition by a novice user in Data Management depending on the user profile.
- Automatic patient numbering:
  - By study number + center number + sequential patient number (with the possibility of including existing preset study/center numbers)
- Screen to review the Audit Trail data.
<table>
<thead>
<tr>
<th>Feature</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product is email enabled.</td>
<td></td>
</tr>
<tr>
<td>Audit Log facility for CRF modification traceability.</td>
<td></td>
</tr>
<tr>
<td>User friendly data Import/Export interface:</td>
<td></td>
</tr>
<tr>
<td>- System for exchanging data between databases</td>
<td></td>
</tr>
<tr>
<td>Spell Checker.</td>
<td></td>
</tr>
<tr>
<td>Customizable error/warning messages:</td>
<td></td>
</tr>
<tr>
<td>- Associated at field level (activated by moving from one field to another)</td>
<td></td>
</tr>
<tr>
<td>- Associated at page level (activated by clicking on save button)</td>
<td></td>
</tr>
<tr>
<td>Flexible error messages definition:</td>
<td></td>
</tr>
<tr>
<td>- Stop message (blocking)., - Warning messages (not blocking).</td>
<td></td>
</tr>
<tr>
<td>Ability to store screen failures in the database.</td>
<td></td>
</tr>
<tr>
<td>Flexible record data entry screen definition:</td>
<td></td>
</tr>
<tr>
<td>- Tabular form, - Full screen form</td>
<td></td>
</tr>
<tr>
<td>Page (screen) navigation:</td>
<td></td>
</tr>
<tr>
<td>- Page by page (sequential next and previous page), - Direct access through a full index page</td>
<td></td>
</tr>
<tr>
<td>Index page showing the different CRF page statuses:</td>
<td></td>
</tr>
<tr>
<td>- Never entered, - Entered by site ready for SDV, if applicable, - Reviewed by DM, - Locked by the CRA for monitoring SDV review, if applicable, - Frozen by the CRA or DM, - Locked by the CRA or DM, - Navigation through pages defined by page status</td>
<td></td>
</tr>
</tbody>
</table>

### 5.6 Database Reports

1. **Standard feature of the product in current release.**
2. **Standard feature of the product in further release within the next 12 months.**
3. **Needs a specific modification of the standard version.**
4. **Not supported within the next 12 months.**

Standard system and metrics reports available (please attach list):
- CRF page or module inventory status reports
- Missing page reports, - Outstanding query report, - Query Aging Report, - Query Status Report
- Query Trend Report, - Audit Trail Report (filter by patient number, data field, page number), User Account Report

Ad hoc reports customizable:
- By the DM, - Ease of report generation
- By all users (includes user friendly search by example engine)

Ability of system to interface with:
- MS Access, - Crystal Reports, - SAS

Support of the local format date/number/unit measure.

Print preview mode available.

Save/Run report and its query definition, access through user profiles.

Export report to PDF.
Export report to Excel.
Export report to XML.

Graphic analysis facility (as a part of data review tool).

Ability to convert completed CRFs into PDF format.

Ability to restrict access to reports by roles and user profiles.

Ability to store user generated queries, tracking and versioning of queries.

Ability to publish user queries for other trial team members to use.

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<th>4</th>
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</thead>
<tbody>
<tr>
<td>5.7</td>
<td>Data Monitoring (if CDMS can support EDC)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Standard feature of the product in further release within the next 12 months.
4. Not supported within the next 12 months.

<p>| |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Ability for the CRA or DM to inform, electronically, the site personnel about the detail for each problem found at page/field level.</td>
</tr>
<tr>
<td>Allow the CRA or DM user to deactivate manually for a CRF those queries for which an explanation is provided.</td>
</tr>
<tr>
<td>Ability to change the query result status when the problem has been solved.</td>
</tr>
<tr>
<td>Ability to track Source Document Verification at the field, page or patient level.</td>
</tr>
<tr>
<td>Display of Adverse Events and Medications on one screen.</td>
</tr>
</tbody>
</table>
### 5.8 Data Entry / Global Updates

| 1. **Standard feature of the product in current release.**  
Double Data Entry system to accommodate paper studies.  
Icon or visual cue indicating the data entry status of particular screens/CRFs.  
Feature for indicating that the response to a data field is Not Done or Not Applicable.  
First pass must be performed by a single user (system prevents another user from updating Pass1 that is in progress by another user).  
Second pass must be performed by a single user (system prevents another user from updating Pass2 that is in progress by another user).  
Reconciliation of first and second passes must be performed by Pass2 user or by a third user.  
Arbitration or Verification process displays both the value entered during Pass1 and the value entered during Pass2.  
Arbitration or Verification process allows response other than the responses entered during first and second pass.  
Tool provides access to Protocol and CRF Completion Guidelines.  
Tool has the capability to provide balloon help.  
Ability to configure select fields as single pass entry.  
Option for single pass entry with visual verification for selected pages and/or data fields.  
Capability to randomly select from a set of sites, 10% of the patients as soon as patient enrollment is complete to perform database audit.  
Capability to print CRFs with the patient’s data (for QC Audit use, not listings).  
Ability for global clinical data updates or data deletions.  
Ability to restrict, through database rights and roles, the ability to perform global clinical data updates or data deletions. |  
|---|---|---|---|---|
Ability to test run global updates or deletions prior to implementation of updates or deletions.
Global updates or deletions are captured in the audit trail.

### 5.9 Discrepancy Management

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>2. Standard feature of the product in further release within the next 12 months.</td>
</tr>
<tr>
<td><strong>4. Not supported within the next 12 months.</strong></td>
</tr>
<tr>
<td>Tracking of data query status with the possibility of manual deactivation.</td>
</tr>
<tr>
<td>Ability to store/save query text and resolution text to reuse for manual queries.</td>
</tr>
<tr>
<td>Ability to run checks in online and batch mode. (Batch checks to be limited by status flag, (i.e., limited to patient groups.).)</td>
</tr>
<tr>
<td>Ability to query CDMS by patient, site, etc…</td>
</tr>
<tr>
<td>Ability to check the number of edit checks in the final system before deployment to eliminate redundant checks.</td>
</tr>
<tr>
<td>Change status from query to protocol violations and vice versa.</td>
</tr>
<tr>
<td>Ability for the DM to make self evident changes.</td>
</tr>
<tr>
<td>Ability to print list of all self evident changes.</td>
</tr>
<tr>
<td>Ability to flag protocol violations.</td>
</tr>
<tr>
<td>Ability to restrict who has access to protocol violation listings.</td>
</tr>
<tr>
<td>Ability to add new checks after data entry has started and to run new checks on previous data.</td>
</tr>
<tr>
<td>Discrepancy management available for paper-based trials.</td>
</tr>
<tr>
<td>Discrepancy management module within the front end user interface for easy navigation and resolution of discrepancies that have fired in the system.</td>
</tr>
<tr>
<td>Discrepancy management module should allow for discrepancy views to be sorted by investigational site, by subject, or by CRF.</td>
</tr>
<tr>
<td>Programming features can be easily and quickly learned by a layperson with a good aptitude for programming logic but without extensive programming knowledge.</td>
</tr>
<tr>
<td>Discrepancies can be converted into paper-based data queries or PDFs.</td>
</tr>
</tbody>
</table>
Ability to generate manual queries on a field or at the form level via simple actions (e.g. a few keystrokes or mouse clicks).

Only one discrepancy captured on a printed query page (i.e. One data query per printed form).

Ability to print query drafts prior to a query status of 'Final' or 'Sent'.

Data query format template can be customizable/configurable (to comply with SPONSOR's standard).

Ability of data queries to have status of new, sent, received, and closed (or equivalent).

Discrepancy statuses can be configured such that SPONSOR can create or name its own status (e.g. 'review pending').

Quick link between discrepancy and data screen/CRF page in question.

Visual cues on the data entry screen indicating whether there is a discrepancy on the data field and status of the discrepancy (e.g. relevant data fields highlighted in red if there are active or sent discrepancies relating to that data point).

System back end tracks date of query generation, dissemination, receipt and integration.

### 6 Database Lock/Unlock

1. **Standard feature of the product in current release.**
2. **Standard feature of the product in further release within the next 12 months.**
3. **Needs a specific modification of the standard version.**
4. **Not supported within the next 12 months.**

   - Ability to close/freeze the access to the data for a given study and archive, either at the full study lock, interim analysis or for a subset of data.
   - Ability for locking and freezing tasks to be performed by non-IT personnel assigned with appropriate database rights and roles.
   - Ability to freeze data at page, visit, patient and site level.
   - Ability to lock data at page, visit, patient and site level.
   - Ability to unfreeze data at page, visit, patient and site level.
   - Ability to unlock data at page, visit, patient and site level.
   - Record in audit trail of unlocked items.
   - Ability to generate database snapshots by date ranges.
<table>
<thead>
<tr>
<th>Ability to generate database snapshots by variables.</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ability to generate database snapshot by status flag (locked patients, etc.).</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ability to generate database snapshots by patient.</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>
### 6.1 Event Tracking and Trial Status

<table>
<thead>
<tr>
<th>Feature</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. <strong>Standard feature of the product in current release.</strong></td>
<td></td>
</tr>
<tr>
<td>2. <strong>Standard feature of the product in further release within the next 12 months.</strong></td>
<td></td>
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<tr>
<td>3. <strong>Needs a specific modification of the standard version.</strong></td>
<td></td>
</tr>
<tr>
<td>4. <strong>Not supported within the next 12 months.</strong></td>
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</tr>
</tbody>
</table>

- Module to track received CRF forms that are pending entry.
- CRF tracking date received is recorded in the backend table and this information can be easily accessed by SPONSOR through reports.
- Audit trail captures CRF tracking information including date, time stamp and username of person who performed tracking task.
- Tracking information recorded able to be modified/deleted as long as data entry has not begun on relevant forms.
- Status of outstanding queries, reports.
- Track missing screens/pages (expected page list vs optional page list).
- Track number of queries by CRF modules and fields being generated by site.
- Ability to flag status at the page, patient and visit level.
- Ability to track protocol amendments and CRF changes.
- Ability to track entry of CRF on Paper Trials (pass1, pass2, verified).
- Ability to track self-evident changes.
- Ability to automatically assign tracking numbers to DCF.
- Ability to automatically track query resolution.
- Online access to outstanding query reports and events that are being tracked.
- Audit Trail compliant with 21CFR11.
- Electronic signature process is 21CFR11 compliant.
- Ability to have one signature per book, but need the flexibility to change if required.
- Ability to track and flag SAEs as reconciled.
- Ability to see that the site is locked after all patients being treated at the site are locked.
- Functionality supports workload and resource forecasts as it serves as a centralized tracking mechanism.
Additional CRF tracking statuses available to note monitoring status or instances where blank CRF pages are received with no data.

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### 6.2 External Electronic Data/Local Lab Data

1. **Standard feature of the product in current release.**
2. **Standard feature of the product in further release within the next 12 months.**
3. **Needs a specific modification of the standard version.**
4. **Not supported within the next 12 months.**

- Ability to load external data and display on screens with an ability to restrict this display if required.
- Ability to have screens to enter additional data (e.g., comment on data at a field level for flagging clinical and non-clinical significance) and restrict the display if required.
- Ability for edit checks to be run against batch loaded data.
- Ability to load different sources of CDM data.
- Centralized coding (i.e., Normal Lab Values/Ranges) to manage upload of external data.
- Tools for gaining efficiency in applying local reference range to particular sets of data.
- Ability to Export and Import data based on CDISC standards.
- Ability for a site to choose lab ranges from multiple local labs.

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### 6.3 Dictionary Coding

1. **Standard feature of the product in current release.**
2. **Standard feature of the product in further release within the next 12 months.**
3. **Needs a specific modification of the standard version.**
4. **Not supported within the next 12 months.**

- Auto-encoder for concomitant medication and AEs supporting multiple coding dictionaries.
- Flexibility to access multiple dictionaries.
Version control feature for dictionaries.
Self learning tool for coding (checks historical/expert coding and learns).
Allow multiple staff to code at the same time.
Auto encoding and Manual coding features.
Ability to run consistency listings of coding.
Auto-encoder supports MedDRA.
Auto-encoder supports WHO DRUG.
Ability to maintain synonym list.

6.4 Rights and Roles / Database Administration

<table>
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<tbody>
<tr>
<td>2. Standard feature of the product in further release within the next 12 months.</td>
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<tr>
<td>4. Not supported within the next 12 months.</td>
</tr>
</tbody>
</table>

Database administration can be performed by Senior Data Manager personnel or non-IT management staff.

The following roles exist for paper based trials:
- Data Entry Pass 1, - Data Entry Pass 2, - Data Manager, - Biostatistician, - System User
- Database Administrator, - View Only

The following roles exist for EDC trials (if applicable):
- Trial Manager, - Data Manager, - Database Administrator, - Biostatistician, - Database Developer, - CRA, - Site Coordinator, - Primary Investigator

Flexible workflow modification.

Ability to generate a report listing all users who have accessed and modified data (audit trail print out).

Ability to define roles and responsibilities for tasks.

Ability to provide field level access rights assignment.

Available tasks to be assigned contain equivalents to the following:
- creation of roles and users, - view roles and users, - delete and activate roles, - suspend or delete users, - generate and edit data queries, - view data queries, - print queries, - answer/close queries, - create reports view, - update or delete reports, - view and print subject data, - create and set-up sites, - change or delete sites, - enroll subjects, - edit subject information, - create
unscheduled visits, - enter data into data entry screens and add notes, - change data without a query, - delete data of subject, visits, or modules, - delete subject from system, - lock and unlock subject data, - track CRFs, - adjudicate CRFs post pass 2 entry, - indicate monitoring status of e-CRFs (EDC only). \textit{(PLEASE SPECIFY which tasks can not be assigned.)}

7 Technical Architecture and Operational Environment

Provide responses to the following questions:

a) What are the client software requirements (e.g. Operating System, browser…etc.) to use the product?
b) Are there any additional components (Java applets, cookies, ActiveX controls…etc.) to be installed at the site if it’s a browser based environment?
c) Provide overview of product architecture (enterprise standards, security …).
d) Provide an overview of Scalability and Performance of the product.
e) Provide details of the software components and technology stack (e.g. OS, Database, Middleware… etc.) that will be used for this solution.
f) What core technologies have been used to develop the product?
g) How flexible and open is the product to integrate with other applications (e.g. APIs, Web services... etc.)? Please provide the available system functionality in order to integrate with external systems such as IVR and Labs.
h) Provide overview of product strategy (direction and commitment).
i) Does the product interface with any widely known CTMS (Clinical Trial Management Systems)? Or, does product contain CTMS functionality? If no, is this planned for the future?

8 Technical Support and Training

a) Provide responses to the following in relationship to technical support and training:
b) List the Countries where technical support is available.
c) List the Languages where the technical support is available.
d) Indicate whether telephone and email support is available.
e) List the languages supported and the hours of operation.
f) The total number of employees permanently assigned to the Help Desk response line. Specify number of Permanent, Contract and Outsourced.
g) Describe the technical support escalation procedure and timelines.
h) Explain the bug reporting, documentation and resolution procedure including the minimum response time.
i) Average amount of training recommended for end-users, data managers, system administrators and application developers.
j) Train the trainer program availability for CRA, Site and DM functionality.
k) The guaranteed response time for service and support. What are the Service Level Agreements?
l) The level and amount of on-site training and support provided under existing contracts.
m) The cost, location, duration, frequency and description of provided training courses.
n) Training and Implementation: include a suggested implementation schedule for the following implementation phases: user training; product delivery and implementation including customizations, if needed, and user testing of all application components in parallel or as applicable..
o) List courses scheduled for this year or attach list of available courses.
p) Is e-learning available with the product? If yes then please list the modules available.

9 Documentation
Provide responses to the following in relationship to user support documentation.
  a) Details of the system documentation that will be included.
  b) Details of the application developer documentation that will be included.
  c) Details of the user documentation that will be included.
  d) Details on the format and access to this documentation.

10 Security, Confidentiality and Audit Trail
Describe the methodology used by your product for system security and electronic signatures:
  a) User identification when accessing a study database (e.g., login username and password, password management).
  b) Trial site users for e-signing patient visit data or a set of data modified by user.

Describe the following processes and/or system functionality in relationship to system security, confidentiality and auditing:
System Functionality for:
  a) Audit Trail
  b) Electronic Signature
Procedures for:
a) Group security assignment and management  
b) Backup and restore  
c) Disaster Recovery/Business Continuity (including data hosting capabilities, redundancy, and facility security)

System Status:

a) List all currently known hard and soft limitations of your product