edc management℠
education
integration
evaluation

edc today™

A Technical Bulletin Published by EDC Management Issue No. 7

Based on research by:
Kirk Mousley, PhD and
EDC Management

Written by:
Anne Jacobson, MPh

In the next issue of ***EDC Today:***

Reaping the Rewards: Leveraging Your Investment in EDC

About EDC Management:
EDC Management was founded to assist biopharma companies plan, prepare for and implement Electronic Data Capture (EDC) strategies according to their data management goals and objectives. We do not sell or endorse any specific EDC software application or vendor.

EDC Management
P.O. Box 384
Conshohocken, PA 19428
484-530-0300 (voice)
610-567-0357 (fax)
info@edcmanagement.com
www.edcmanagement.com

10-07-02-4150

EDC and Data Entry Systems:

What System Developers Need to Know

Welcome to our seventh issue! EDC Today is an independent publication about current information and issues in Electronic Data Capture (EDC) strategies and technologies for the Biotechnology and Pharmaceutical (biopharma) industry. Each month we examine topic areas related to EDC theory, technology, practice, or implementation.

EDC promises to create cleaner data faster, in part by bringing data entry to the investigator site, where erroneous data can be identified and reconciled in real time. Critical to the success of any EDC system is the performance and functionality of the data entry system (DES). In this issue, we explore the impact of EDC on the data entry system developer (DESD).

Testing of new drug candidates is an increasingly complex, lengthy and expensive process. Clinical testing alone now costs more than $100 million, with large-scale Phase III studies typically costing between $2 and $30 million each. Each day's delay in getting to market is estimated to cost $1 million in lost revenues.[1]

In a paper-based study, the time to database lock from last subject last visit (LSLV) is typically 8 to 10 weeks. This milestone depends on three processes: retrieval of the last CRF in house, entry of the final data, and resolution of the last outstanding query.

EDC technology improves the efficiency of each of these processes, thus significantly reducing this critical time period. First, because data are entered at the study site, when the last CRF is entered at the site, the last CRF is received in-house. Second, EDC reduces both query turn-around time and query volume. Finally, in the electronic environment, data edit checks and validation checks can be hard coded into the electronic CRF (eCRF). As a result, these issues are raised immediately and significant delays can be avoided.

Some estimates suggest that EDC should be able to reduce the database lock time from LSLV to 1-5 days, including the time required to transfer databases from the EDC application to the clinical database.[2] Critical to achieving this goal is the development of an optimized data entry system.

Creating Data Entry Systems

Traditionally, the overarching design philosophy of clinical DESs is known as "heads-down" data entry, meaning that staff enter CRF data from paper to the Clinical Data Management System (CDMS) database without altering any CRF information. In other words, staff members were not free to fix or flag errors as they entered data. As a result, data were cleaned only after being entered into the database. Post-entry data cleaning queries were run against the database and any detected discrepancies were managed later.

With EDC, entry of clinical trial data is moved to the investigator sites, in many cases eliminating the paper CRF. With this change, the traditional way of cleaning the data – reconciling errors only after data are in the database – is no longer appropriate. Instead, edit checking is moved from post-entry to the time of entry and ideally, only 'good' data are allowed into the database. Obviously, the EDC system will still need to accept whatever data the site enters, but will flag those errant values for later resolution.

The role of the DESD is to create a DES that facilitates this process. When designing a system, the DESD must consider a variety of relationships, or interfaces, that are unique to the EDC environment. The DES must also include principles of good graphical user interface (GUI) design. The development of the DES will alter some of the traditional timelines and milestones of trial preparation.

Interfaces Unique to EDC

EDC systems introduce a range of new interfaces into the data management process. For example, when using EDC, investigator site personnel must interact with new data entry and tracking systems that were not used in the paper-based process. Indeed, under EDC, investigator site personnel must interface with computer systems, computer systems must interface with each other, and site personnel must interface with CRAs and Study Monitors – all in new ways. Typical interfaces in the EDC environment are summarized in Table 1.

(continued on page 2)

Table 1. Interfaces in the EDC Environment

Human/System Interfaces:

- Investigator site user to the DES GUI and navigation features
- Developer to EDC development system, possibly new scripting language(s) and form development tools, and new IDE
- Investigator Site User to TS
- Study Monitor(s) and CRAs to DES
- Study Monitor(s) and CRAs to TS
- CDM to DES
- CDM to TS

System/System or System/Data Interfaces:

- Bridging to other systems (e.g. Accounting, Study Agent Handling (i.e., drug tracking and shipping))
- Downloading and/or uploading handling/processing
- Auto-encoding (e.g., prior concomitant medications, adverse experiences)
- Other derivations (e.g., laboratory result high/low flagging and standardization of units)

Human/Human Interfaces:

- DESD to Project Management
- DESD to CDM and CRA (Editing Ground Rules)
- DESD to Dictionary/Codelist Maintenance
- DESD to IT support
- DESD to EDC Vendor
- CRA to Investigator Site Personnel

Legend: CRA = Clinical Research Associate; CDM = Clinical Data Manager; DES = Data Entry System; DESD = Data Entry System Developer/Designer; IDE = Interactive Development Environment; GUI = Graphical User Interface; TS = Tracking System

When designing an EDC system, the DESD must consider these interfaces and how each will shape the DES. For example, one critical human/human interface is the sponsor's DESD to the EDC vendor. If the EDC system is configured under the full-service application service provider (ASP) model – wherein a DESD at the vendor develops the DES – the sponsor's DESD will no longer develop the entry system in-house. Instead, the sponsor's DESD will write technical specifications for the vendor-produced data entry system and for the data transfer file(s). Sponsor personnel may also manage the details of integrating new systems and data with legacy systems.

Though the DESD will likely come from a traditional information technology (IT) background, it is critical for the DESD to be familiar with the subtleties of EDC. For example, because data are captured by different electronic means in many EDC environments, greater awareness of alternate forms of data capture may be needed. Patient diary information may be captured by personal handheld device, whereas results of laboratory assays performed by a central lab may be sent to the sponsor via electronic transfer. Awareness of form factor issues and different scripting languages may be needed in order to develop, and/or successfully integrate with, systems on hand-held and other electronic platforms.

Real-time Error Detection

A prime advantage of eCRFs is that data can be cleaned as it is entered, often during the clinical study visit. With errors detected in real time, corrections can be made with the patient present.

Detecting errors during entry becomes an important design goal for the entry system developer. DES developers should know what to do when a problem arises – for example, when erroneous data are detected during a data entry session. Error detection can be facilitated by the inclusion of a series of data edit checks. Common data checks are summarized in Table 2.

Even with EDC, some back-end edit checks may still be needed (e.g., Serious Adverse Event reconciliation). Implementing these edit-checks may be a challenge depending on the architecture of the EDC system and its features. In any event, how the edit checks are written and executed will depend on the EDC product.

The DESD may also need to be more concerned about security. For example, user account maintenance activities will need to be performed in order to permit investigator site personnel to access data entry and editing functions.

Table 2. Typical Data Edit Checks

Complexity	Data Check	Examples
Low	Data type	Field is a date, a number, or one or more characters
	Data format	Text case, field masks, and/or date format
	List of values	List member, codelist, or dictionary
	Range checking	The entered value is between, less than, or greater than one or more values
	Check digit	The 10th digit in a VIN can be generated algorithmically from the first 9 digits
Moderate	Validity depends on another field's value	Pregnancy test result of "Yes" for male patients
	Validation on computed value	Range check of weight in kilograms where the data are entered in pounds
	"Other" checked, specify value	Value specified, "other" not checked
High	Cross-form dependencies	Date of birth should be before laboratory assay sample date
	Auto-encoding failure	"Haedache" not auto-encoding because of misspelling
	Derivation failures	Failure to high/low flag a laboratory value
	Clinical assessment required	A lab value that would be considered out of range in a healthy person may be reasonable for someone with a known heart condition

(continued on page 3)

Design Considerations

Minimizing the investigator site personnel's data entry frustration should be an important goal of DES design. Indeed, the DES should be as easy to use as a pen and paper form. In their article, “Concepts of User Interface Design”, the Common Front Group at Cornell University describes the importance of considering the user's experience and the distinction between learn-ability and usability:

> “Many people consider the primary criterion for a good user interface to be the degree to which it is easy to learn. This is indeed a laudable quality of any user interface, but it is not necessarily the most important. The goal of the user interface should be foremost in the design process. Consider the example of a visitor information system located on a kiosk. In this case it makes perfect sense that the primary goal for the interface designers should be ease of operation for the first-time user. The more the interface walks the user through the system step by step, the more successful the interface would be.”[3]

Ideally, data entry systems should support, extend, supplement, or enhance – but not replace – the user’s skills, background knowledge, and expertise. For example, when creating systems for expert users, frequent system usage, or systems with frequent slow response times, system designers might elect to use fewer screens that capture more data per screen. Likewise, when creating systems for novice users, infrequent system usage, or systems with fast response times, system designers might elect to use more entry screens with less data captured per screen.

To provide flexibility and to serve a wider user community, product developers may want to incorporate a lot of functions into DES. However, unless considerable effort is devoted to the design of the user interface, extensive technological sophistication may be daunting to users. The U.S. Food and Drug Administration (FDA) has identified common problems of software systems that can lead to errors:

“ • Illogical or cumbersome control sequences
- Unfamiliar language, symbols, or codes
- Inconsistencies among display formats
- Conventions that contradict user expectations
- Uncertain or no feedback after input
- Functions that are hidden from the user
- Missing or ambiguous prompts, symbols, or icons
- Unsignalled resets or defaults
- No status information
- Missing lock-outs or interlocks
- Requirements for complex mental calculations”[5]

When using unfamiliar systems, users can become frustrated by cumbersome data entry steps and make errors not directly related to those steps. Because one of the primary advantages of EDC is the reduction of erroneous data, it is important that the data entry process does not introduce new errors. It is also important that new help features be worded so the intended audience – such as investigator site personnel – can make full use of the help provided. Ambiguous abbreviations or acronyms used in menus, commands, or help functions introduce serious data entry errors. For example, “IM” might mean “instant messenger” to the developer but mean “intra-muscular” to investigator site personnel. Therefore, the DESD should be fluent in the study-specific language used by investigator site personnel. If the clinical trial is global in nature, the EDC system is most likely to be successful when the developer is able to work with multiple languages (i.e., the “questions”, help files, and the like may require translations into other languages).

The FDA offers the following design strategies for preventing many software-related errors:

“ • Do not contradict the user's expectation. Rather, exploit their prior experience with computerized equipment and consider conventions related to language and symbols.
- Be consistent and unambiguous in the use and design of headings, abbreviations, symbols, and formats.
- Always keep users informed about current device status.
- Provide immediate and clear feedback following user entries.
- Design procedures that entail easy-to-remember steps.
- Use prompts, menus, etc. to cue the user regarding important steps; do not “strand” the user.
- Give users recourse in the case of an error. Provide conspicuous mechanisms for correction and trouble-shooting guides.
- Do not overload or confuse users with information that is unformatted, densely packed, or presented too briefly.
- Consider the use of accepted symbols, icons, colors, and abbreviations to convey information reliably, economically, and quickly.”[5]

When designing systems, checklists may be a valuable resource for optimizing user experiences and reducing the likelihood of error. To help system developers improve users’ experiences, Deniese Pierotti of the Xerox Corporation in Stamford, Connecticut, developed an extensive checklist as a guide for evaluating user interfaces.[4] Table 3 summarizes the 13 major categories into which the 100+ checklist prompts fall.

System Development Planning and Timelines

Certain system development milestones will shift with the implementation of EDC. Though final protocol approval and design and production of the CRFs are critical prerequisites of any study, with a paper-based study, database set-up and testing does not need to be completed, nor does the validation checks and data handling plan, before first-subject-first-visit. Therefore, due to time constraints, traditional paper-based studies often begin before all data management set-up activities are completed.

In contrast, with an EDC-based study, data cannot be collected until the EDC database is fully built and tested, and all the edit checks and validation checks are defined and integrated. Therefore, a study conducted using EDC requires database set-up, testing, and validation to be completed before the study begins. This change has significant resource and process implications for system developers.

Usability Testing

Another critical aspect of system development is testing for ease and accuracy of use, which is often called usability testing. Usability testing is the only way to ensure that users can effectively install, maintain, and operate systems. For optimal results, the user interface should be tested under conditions that are as realistic as possible.[5]

(continued on page 4)

Table 3. Checklist for Evaluating User/System Interface

Prompt Category	System Design Goal
Visibility of System Status	Through appropriate feedback and within reasonable time, systems should keep users informed about system status.
Match Between System and the Real World	Instead of using system-oriented terms, systems should speak the user's language, with words, phrases and concepts familiar to the user. Communication should follow real-world conventions and present information in a natural and logical order.
User Control and Freedom	Rather than having the system dictate processes, users should be free to select and sequence tasks when appropriate. Because users occasionally choose system functions by mistake, they will need a clearly marked "emergency exit" to leave the unwanted state without having to go through an extended dialogue.
Consistency and Standards	Users should not have to wonder whether different words, situations, or actions mean the same thing. Follow platform conventions.
Help Users Recognize, Diagnose, and Recover From Errors	Error messages should be expressed in plain language and avoid error codes.
Error Prevention	Systems should be built with careful design that strives to prevent problems from occurring in the first place.
Recognition Rather Than Recall	The user should not have to remember information from one part of the dialogue to another. Instead, instructions for system use should be visible or easily retrievable whenever appropriate.
Flexibility and Minimalist Design	Systems should cater to both inexperienced and experienced users by allowing users to tailor frequent actions. For example, accelerators – which may be unseen by the novice user – may speed the interaction for the expert user. Systems should also provide alternative means of access and operation for users who differ from the "average" user in physical or cognitive ability, culture, language, or the like.
Aesthetic and Minimalist Design	System communications should not contain irrelevant or rarely needed information. Extraneous information competes with the relevant messages and reduces their relative visibility.
Help and Documentation	Though it is often better when systems can be used without documentation, help and documentation may still need to be provided. Help and documentation should be easy to search, focused on the user's task, list concrete steps, and should be a manageable size.
Skills	Systems should support, extend, supplement, or enhance – but not replace – the user's skills, background knowledge, and expertise.
Pleasurable and Respectful Interaction with the User	Interactions with the system should enhance the quality of the user's work-life. Accordingly, the design should be aesthetically pleasing, with both artistic and functional value.
Privacy	Systems should help users to protect personal and/or private information.

User Training

User training requirements will change significantly under an EDC process. For paper-based studies, site personnel need to know what information is being asked for and how to enter it on the paper CRF. For EDC, these persons need to know how to enter the data into the EDC data entry application. Investigator site personnel will need sufficient training on the EDC system in order to use it properly and effectively.

In the EDC environment, significant time needs to be devoted to training. System training will be required before the study for all users and during the study for new or infrequent users. Each person at the investigator site should have documented evidence that they have been trained to use the EDC data entry application. Michael Rosenberg, MD, MPH, President and CEO of Health Decisions, Inc., describes his experience with implementing EDC systems:

"These systems demand a moderate degree of computer familiarity, and training is a part of every study. We have found, however, that after training, the vast majority of users come to strongly prefer this system, to the point where they are reluctant to return to traditional methods. The capability of closely monitoring the performance of even individuals and sites can be used as a means of reinforcing training, with supplementation or additional training, or other resources as appropriate. Ultimately, the continuous and very quick stream of feedback markedly improves site efficiencies."[1]

System Validation and Support

System validation is the process of ensuring that the system functions in the required manner on each piece of hardware used in the study. The DESD should consider how and under what conditions the DES will be validated.

(continued on page 5)

For example, some EDC users prefer to distribute the application on uniformly pre-configured laptop computers. This has the advantage of preventing additional applications from being run or installed, and hence all possible interactions with other software are controlled and eliminated. In addition, in this scenario, both full software and hardware support can be provided, facilitating fault diagnosis.

EDC systems require support with help desk staff available to troubleshoot at any time, 24 hours per day, 7 days per week, particularly in multinational studies, which may span many time zones.

Conclusion

With EDC, personnel at investigator sites enter data directly into electronic CRFs with the use of PCs, laptops, or portable data assistants (PDAs) such as palm pilots. EDC software automatically flags errant or out-of-range data, prompting investigator site personnel to make data corrections or clarifications. Validated data is then transmitted from the investigator site to the sponsor's central database, usually via the Internet.

Critical to the success of EDC is the use of efficient data entry systems. Data entry system designers must consider a variety of factors, from general design principles to the impact interfaces unique to EDC environments. DESDs must also have a thorough understanding of the specific needs of the user population: CRAs, study monitors, and investigator site personnel.

With new and revised features being placed in the data entry system, the developer will need to be sure additional time is allotted for the additional development and testing. Accordingly, milestones in the study development must be shifted. The DESD plays an important role in shaping these revised timelines.

By providing a more efficient means of data management, EDC promises to accelerate clinical development and shorten time to market. EDC addresses the major drawbacks of the paper-based process by moving both data entry and data validation to the source of the data: the investigator site. With optimal data entry systems, EDC is more likely to fulfill its promise of cleaner data faster.

Who's behind the research?

Our lead researcher, Kirk Mousley, PhD received BS and MS degrees in Electrical Engineering from MIT and a PhD in Computer Science from Lehigh University. He has been the President of Mousley Consulting, Inc. since its founding in 1993 and has directed the company's efforts in the areas of clinical database design, data editing/cleaning, document management, and submissions.

Karl Mousley received his BS in Mechanical Engineering from Rose-Hulman Institute of Technology and a MS in Computer Science from Villanova University. He has been a senior member of the technical staff at Mousley Consulting, Inc. since 1993. Among his significant accomplishments are the investigation, evaluation, and implementation of new computer technologies for clinical data management systems and developing strategic plans for integrating these technologies into current systems. He has extensive experience preparing Standard Operating Procedures (SOPs).

References:

[1] *Rosenberg, Michael and Bowden, Michael. Accelerating Drug Development with an Integrated Electronic Approach. European Pharmaceutical Contractor. August 1998, pages 56-64.*

[2] *Byrom, Bill. Managing Clinical Trials via the Internet. Pharmaceutical Physician, March 2001.*

[3] *Cornell University Common Front Group. Concepts of User Interface Design. 1995. http://cfg.cit.cornell.edu/cfg/design/concepts.html. Accessed October, 2002.*

[4] *Pierotti, Deniese. Heuristic Evaluation - A System Checklist. http://www.stcsig.org/usability/topics/articles/he-checklist.html. Accessed October, 2002.*

[5] *U.S. Food and Drug Administration. Do It By Design: An Introduction to Human Factors in Medical Devices. http://www.fda.gov/cdrh/humfac/doit.html. Accessed October, 2002.*

See back for order information.

edc management[SM]
education | integration | evaluation
P.O. Box 384 | Conshohocken, PA 19428
www.edcmanagement.com

edc**today**
Issue No. 7

EDC Today and ***EDC In Depth***

EDC Management publishes well-researched, timely information about EDC technologies and processes. Our technical bulletin, *EDC Today*, overviews a group of related in-depth research reports, *EDC In Depth*.

An annual subscription to *EDC Today* is $175/year and can be purchased via downloadable electronic version or paper version sent via mail. Electronic versions of back issues may be purchased individually for $25 each.

Each *EDC In Depth* research report comes with an executive summary and may be purchased individually for $395 or as a group of related reports for $975. Available in electronic or paper version.

To subscribe to *EDC Today* or purchase a specific *EDC In Depth* research report:

Order online at
www.edcmanagement.com

Email us at
info@edcmanagement.com

Call us at
1-484-530-0300

EDC Management is a consulting and information company offering EDC consulting, including vendor selection, validation and compliance, and site assessment; Clinical and Data Management consulting; hands-on education and training; and EDC publications. Improve process today; position for tomorrow.