Society for Clinical Data Management
DATA DRIVEN

Data Basics

To advance excellence in the management of clinical data

A PUBLICATION SUPPORTED BY AND FOR THE MEMBERS OF THE SOCIETY FOR CLINICAL DATA MANAGEMENT, INC.

Volume 15, Number 1 | 2009 Spring

Letter from the Editors

Arthur R. Shaw, CCDM and Frank McDonald

The importance of designing a database that most effectively captures all the clinically necessary trial information has always been the forefront of data management's initiatives.

With emerging technologies there are many more options available to data management on how to approach a database build. Whether to conduct a paper study, have electronic data capture performed by the site coordinator or even have a system in which data entry is automatically executed with no source documentation verification required, since the data is real time and directly imported from medical equipment. With each new study the data manager and study team must ascertain which route is most appropriate for the specific study.

Another aspect of how to approach a database build comes from the origins of a strong protocol. As explained in "From Protocol to CRF: Protocol Authoring Techniques That Lead to Cohesive Case Report Forms." A strong protocol will become a solid foundation from which to create concise case report forms and this will lend its hand to an accurate database.

The articles in this edition of our newsletter highlight the different types of data collection and database build and the approaches to each one. We are interested in your comments and questions. Please feel free to contact us at info@scdm.org.

From protocol to CRF: Protocol-authoring techniques that lead to cohesive case report forms

Kyle Hart, CCDM, Data Manager/Technical Writer, RS Medical

Designing case report forms (CRFs) is an ambitious endeavor that attempts to distill a clinical protocol into its most fundamental application: The individual forms and fields that capture the events of the trial. Frequently complex, dense documents, protocols contain the rants and ravings of prior investigations, descriptions of diseases, study methods and statistical plans. How can we translate these complicated narratives into something as simple as "Enter blood pressure here?"

Ideally, CRF designers and protocol authors will work collaboratively to develop the protocol concurrently with the CRFs, as a part of the study-design process. When protocol authors and CRF designers both work with a mutual study design in mind, they are more likely to develop compatible documents. Conversely, when a CRF designer is working from a completed protocol, already set in stone, there is no room left for altering the study design based on the lessons learned during CRF development. Drafting the forms and laying out fields on a page helps the CRF designer to visualize the study and the chronology of events that study coordinators will go through to capture data. In other words, designing the forms puts the designer in the shoes of the study coordinator. This frequently brings to light problems with the study design that might not yet have come

Continued on page 3

This Issue

Directory of Advertisers

Letter from the Chair

Linda M. Talley, CCDM

A Great Start for SCDM:

It is hard to believe that the first quarter of the year is already behind us! As we move into Spring and the changing of the seasons, we too, are experiencing wonderful changes in our organization as well! I am excited to share with you some highlights of achievements in the first quarter of 2009:

Committees Restructuring - Based on SCDM's 2009-2012 strategic goals, committees have been reorganized into taskforces and consolidated under three new committees. This has allowed us to improve communications among working groups, eliminate duplication of work, and cross collaboration amongst committees.

We now have 5 new Committees overseeing 9 Taskforces; the Nominating, Finance, Education, Products and Services, and Marketing and Communications. (see page # for more details about the new committee structure and volunteer opportunities).

Membership Renewals – So far in 2009 we have more than tripled the amount of members who have renewed their membership from 1188 in the first quarter of the 2008 renewal period compared to 322 in the same period in 2008. We are hopeful that members are seeing the value in continuing their membership with SCDM. It is our goal to continue to find more ways of making your membership value added, especially during tough economic times. Stay tuned for more details…

CCDM® Certification – We have also seen a record increase in the amount of applications and new CCDM®s in 2009 so far. We nearly doubled the amount of new domestic applications in the first quarter of 2009 from 12 to 22. We have also seen leaps and bounds with the amount of international new applications in the first quarter of 2009 from 1 to 42. We also have 41 new CCDMs® so far this year. We will continue to find ways to increase the amount of CCDM®s and market the value and ROI for CCDM®s in the workplace.

Strategic Directions – In 2008 the Board of Trustees launched strategic priorities to a whole new level for SCDM. Much planning and reorganizing was done to make sure that the Board was thinking and acting strategically when making decisions and setting policies for SCDM. In 2009 we are moving forward on implementing many of the strategic goals that were put in place in the prior year. One of the strategic priorities that has been identified for SCDM is increasing our external partnerships. The SCDM Board has been spending a lot of time identifying key organizations whose programs and services complement SCDM's. Through the newly formed Strategic Directions Committee, SCDM's leaders are working collaboratively with the leaders of these identified organizations to see how we can work together in more efficient and cost effective ways. Ultimately, our goal is to share the value and experiences that SCDM brings to the table with others and bring what they have to offer to our members.

SCDM Going Global – In the past few years SCDM has seen a great interest from international members in our products and services, particularly the GCDMP. With the ramifications of outsourcing and mergers in the Clinical Trials community, SCDM cannot help but to respond to the need to become more global in scope. We are currently exploring ways on how to become a global organization, through our programs, services and partnerships. We hope to share more in the future about our plans to go global as we continue to move ahead with our research and planning.

I am so proud of what we have been able to achieve in the first quarter of this year and want to personally thank all who have been involved in making this a reality! I look forward to what we can continue to achieve together moving forward!

Cheers,
Linda

Society for Clinical Data Management
DATA DRIVEN

2009 SCDM Committees

Education & Professional Development
Michelle Meany
Phone: 908.740.7471
michelle.meany@spcorp.com

Pat Stetser, CCDM
Phone: 267.305.8489
patricia.stetser@accenture.com

Marketing & Communications
Nelson Lee, CCDM
Phone: 650.225.2121
lee.nelson@gene.com

Michael Loftus
info@scdm.org

Products & Services
Jennifer Duggan, CCDM, CCRP
Phone: 416.622.2324 x7249
j.duggan.m@gmail.com

John Estrada
Phone: 925.355.3010
estrada@nextrials.com

Strategic Directions
Anthony Costello, CCDM
Phone: 530.753.4366
dognobble@gmail.com

From protocol to CRF: Protocol-authoring techniques that lead to cohesive case report forms

Continued from cover

up. A collaborative process encourages the stakeholders to identify and resolve problems early in the study-design process.

Protocol authors can structure protocols to maximize their usefulness to CRF designers and, more importantly, to create consistency between the two documents and clarity for readers. For example, most protocols follow outlines that include sections on prior investigations, objectives, trial design, subject population, interventions and statistical plans[1]. To this simple recipe, adding a section that lists and describes all of the assessments that will be used in the study provides CRF designers a single place to look for everything that should appear on the CRFs. This model also eliminates the need to repeat descriptions of assessments every time they occur during a discussion of subjects' progression through study time-points.

From the perspective of the CRF designer, there is perhaps no section of the protocol more crucial than the section on objectives and endpoints. The assessments section (and, subsequently, the CRFs) should be drafted with the endpoints foremost in the author's mind. The study design should generally include no assessments that do not specifically answer an endpoint[2]. In *eClinical Trials: Planning & Implementation*, R. Kush, et al[3], make the case that "the database must document the relationship between the original study protocol and the procedures actually followed for the study, and must be able to support generation of analyses that will be useful to evaluate the study hypotheses." When designing CRFs, the rule of thumb is to omit anything that will not be analyzed at the end of the study. The high costs of collecting superfluous data may include a reduction in the quality of the critical data points.

In describing assessments, protocol authors should be specific. When a study makes use of a standardized or validated survey, authors should include the full name of the survey, the version number to be used and any other version- or edition-specific details, such as the body system for which the survey should be configured.

For tests, scans and functional assessments, authors should describe all equipment that will be used to take measurements, including brands and model numbers–in most cases, they should be the same for all investigator sites. In some cases, different brands of the same instruments may take measurements using different units, or they may even require a different number of fields to capture their results. CRF designers can use brand and model information to obtain brochures and other product details. Together with a description of how the equipment will be used, these details create a clear picture of how investigators will perform the assessments–and the most natural for them to capture the resulting measurements.

Protocol authors should clearly indicate when each assessment will occur. Including a table that displays the study schedule, with the procedures and assessments clearly identified for all study milestones, makes the protocol easy for readers to visualize and provides CRF designers a simple checklist for every time-point.

Well-designed CRFs that accurately represent their protocols will encourage investigators and study coordinators to follow the protocol's prescribed procedures. This consistency, from protocol to CRF to data capture, leads to improved quality of the study data. ■

References

1. *United States Food and Drug Administration. ICH-E6: Good Clinical Practice: Consolidated Guidance. 1996.*
2. *Data acquisition. Society for Clinical Data Management. Good Clinical Data Management Practices. 2007:15-23.*
3. *Data Quality and Data Integrity. In: Kush RD, Bleicher P, Kubick WR, Kush ST, Marks R, Raymond SA, Tardiff B. eClinical Trials: Planning & Implementation. Thomson CenterWatch, 2003:108-113.*

Kyle Hart, CCDM, is a data manager and technical writer at RS Medical in Vancouver, WA, where he oversees data management for device trials and participates in development of clinical protocols, manuscripts and white papers. He has been in the medical device industry for more than four years, and he has been involved in technical writing for eight years.

Build vs. Buy: Considerations for EDC Investment

Ross Rothmeier, Senior Director EDC Portfolio, Covance, Inc.

Companies looking to implement an electronic data capture (EDC) system have a wealth of choices. The 'build versus buy' scenario has been a major point of contention since the EDC industry emerged over 15 years ago. The question is still relevant today as pharmaceutical and biotechnology companies continue to look for opportunities to cut costs and maximize process efficiencies for conducting clinical trials. The question of whether to acquire EDC technology from a vendor or build it using internal capabilities is often at the forefront of long-term strategic decision-making.

Today, a few companies have established themselves as industry leaders, but there are still dozens developing new EDC systems. There are also a few pharmaceutical and biotechnology companies successfully developing their own custom solutions. As EDC continues to grow across the industry through both of these approaches, either of them could be right for your needs. To determine the optimal EDC solution, it is important to carefully consider your company's EDC strategy, corporate culture and budget. This will position you to make the best decision and enable you to realize the benefits EDC can bring to your organization.

Buying an EDC solution typically means getting a license to use a vendor-owned product for a fee. The license fee allows you to use the EDC software to conduct a specified number of trials. Other fees are charged for setup, hosting, helpdesk support and any custom reports or data extracts.

If your needs extend beyond setting up the trial, most EDC vendors do not provide clinical services like data management, monitoring or statistics. For these services, consider your own in-house capabilities or contract out to a contract research organization (CRO) with EDC experience.

Benefits of Buying an EDC Solution

Buying a system developed by an EDC vendor offers the advantage of getting a finished product right away, and deferring maintenance to a company whose core business is developing EDC software. These companies specialize in and have dedicated resources for managing product development and testing.

In addition to the technology, the benefits of working with an established EDC vendor include access to experts who provide services such as:

- Design and development of electronic case report forms (eCRFs), reports and data extracts
- Hosting the application
- Technical helpdesk services for you and your sites
- Archived copies of the data at trial completion

The benefits of working with an established EDC application also extend to your staffing. As vendor products become more established in the industry, they become part of a general skill set for people working on clinical trials. This makes it easier to find data managers, clinical research associates (CRAs), study designers and project managers who are familiar with an EDC product's features and functions. With the accreditation programs available from vendors, you can even recruit for certified people in the industry. Leading EDC vendors also have established partnership programs with top CROs, providing you access to an ever broader breadth of talent.

Challenges of buying an EDC solution

Although there are many advantages to working with vendor-based EDC products, there are some challenges you will need to manage.

Successful EDC implementation is based on process more than product. Features and functions enable processes, but when adopting a technology from a vendor, your processes will have to adapt to the capabilities of the product. Sometimes called "work-arounds," process exceptions can add to the cost and time of implementation. Established vendors may have best practices for study design and development, but processes for trial conduct will need to come from within your organization or, possibly, contracted sources.

Integration with data outside the eCRF can also be a challenge. If you need to incorporate non-eCRF data into your trial and see it in your EDC application, you will need to establish links between your EDC system and the external data source. Data from electrocardiogram (ECG) systems, interactive voice-response/interactive web-response (IVR/IWR) systems, or central labs will probably require some programming effort to convert into a loadable format for the EDC application. In addition, data reconciliation with safety reporting systems may require special programming or development of custom reports to support a reconciliation process. These costs are important to consider when looking at the cost of buying/licensing an application.

Benefits of the 'Build' Option

Building an EDC application is less common in an era where we have established EDC vendors and tightening information technology (IT) budgets. Still, some companies have opted to develop a custom product to meet their defined requirements. In an effort to improve timelines and increase process efficiency, these companies see an advantage in developing a system that meets their specific needs rather than adapting to a vendor-based one. These requirements are ideally based on best practice business processes defined prior to product build.

While basic features and functions of EDC are fairly consistent, integration requirements are not. There are almost as many

Continued on page 5

Build vs. Buy: Considerations for EDC Investment

Continued from page 4

variations in requirements for integrating with other applications as there are companies doing clinical research.

Custom integrations with trial management systems, data warehouses, grants management software and severe adverse events (SAE) reporting applications can yield high efficiency within the operation of your organization. These custom integration opportunities may justify the cost of developing a custom product by incorporating them into the core application instead of paying for and developing them individually.

Developing custom integrations with a vendor-based solution can be a costly endeavor. Although vendor-based solutions enable you to transfer development and maintenance costs to the vendor, custom integrations are usually an extra cost not included in the typical license and maintenance contract for an EDC application.

The build option allows you to determine EDC application changes and enhancements based on your company's needs and priorities, rather than a release schedule defined by a vendor.

Challenges of the 'Build' Option

Software development takes time, and there are plenty of risks associated with developing a specialized application. Just like clinical trials where the protocol and analysis plan are key aspects to keeping the trial on target and within budget, solid requirements and test plans are critical to software development. While pharmaceutical and biotechnology companies apply these skills very effectively to clinical research, they do not always transfer smoothly to software development efforts.

The cost of software development can be high and difficult to accurately predict. This risk should be compared to the relative cost of licensing, customizing and integrating a commercially available product. This comparison helps assess both the cost of acquisition and longer term costs of ownership.

It can be a challenge to find software developers who understand the regulatory and operational needs of clinical research. Consulting and recruiting firms can help. Software developers from the financial industry have comparable skills due to Sarbanes-Oxley compliance regulations that are similar to those found in the 21 CFR Part 11 in the pharmaceutical industry.

Deciding Factors

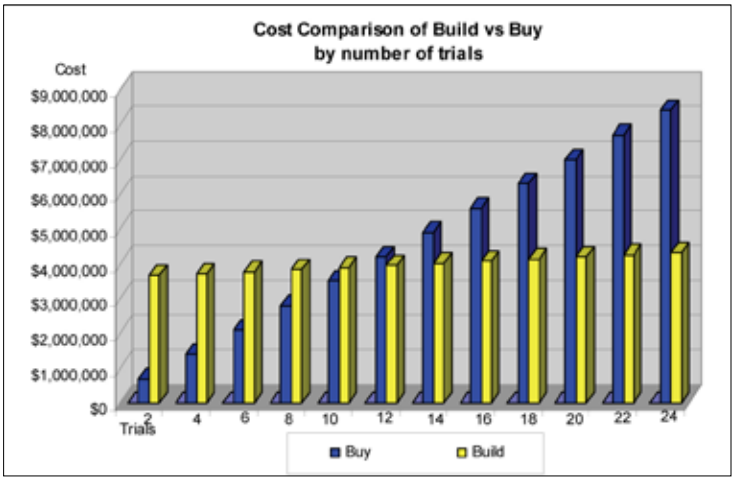
When determining whether to build or buy an EDC application, these key factors should be evaluated in depth:

- **Cost** – The cost of developing a new system vs. the cost of buying one from a vendor
- **Existing products** – Existing vendor products used in the industry
- **IT capacity** – Your company's internal IT infrastructure, resources and experience, including software development expertise

Cost

Whether building or buying an EDC system, you will incur internal costs. These include process engineering, organizational restructuring and redefinition of roles and responsibilities for data managers, clinical research associates, clinical operations personnel, project management and biostatistics.

Because EDC has been fully adopted by companies, it is clear that the cost difference between developing and maintaining an EDC application versus licensing one is directly proportional to the number of trials being conducted.



Source: Rothmeier, 2008

Buying generally implies licensing and paying for services through a vendor in a model known as the application service provider (ASP). License costs will vary by vendor and study. The chart shows the cost of licensing and services related to building average trials based on using an EDC vendor as an ASP provider. Average study sizes vary, but assuming a two-year study with 500 subjects, 50 sites and 200 total forms, vendor prices for ASP services including building, hosting and helpdesk support for the trial would between $350,000 and $450,000.

To develop an EDC system, there are three main factors to consider above what you would need for buying a system:

1) Development staff – Salaries for developers vary, but a reasonable budget for staffing a two-year development cycle with about 10 people would be about $3.6 million
2) Infrastructure – Servers and hardware cost can be estimated at about $100,000 per year, or $200,000 for the same two-year study
3) Study builders – The build model also incurs the expense of creating the trials, which is accounted for in the chart above by assuming .25 full-time employee (FTE) per trial per year.

Continued on page 6

Build vs. Buy: Considerations for EDC Investment

Continued from page 5

With these assumptions, the software development and trial building costs of creating a custom EDC application could be estimated at about $4 million.

From a software development standpoint alone, it could be possible to recoup development costs over time. The more trials done per year, the faster the costs are regained, but realistically it is unlikely to see much return in the first two years.

After building the application, you also need to consider ongoing maintenance and updates to the system. Your strategy, product complexity and IT capacity will drive these costs which can vary widely.

Existing products

There are many EDC vendors in the market, and there is room for debate about which is best. With about half a dozen established EDC vendors servicing the industry, you have a wealth of rich feature sets and companies with solid track records available to you.

Most of these vendors can show how their products provide basic EDC capabilities such as supporting online edit checks, complex trial designs and reporting within a user-friendly interface. Where you may see differences is in how vendors distinguish themselves around their services and ability to integrate with other systems and data sources.

It may be tempting to look at EDC as a commodity, but there are large differences in what additional services and tools vendors have to offer, as well as in the cultures of the vendor companies. A good cultural fit between an EDC vendor and customer is not easy to quantify, but this will have a profound impact on the ability to achieve goals and objectives in a timely and cost-effective manner.

If your needs extend beyond those integration services offered by EDC technology vendors, you may be better served by a leading CRO that has partnered with EDC vendors. These partnerships provide you with an option to use the leading technologies coupled with services and expertise extending well beyond getting an EDC trial up and running.

IT capacity

Nobody would confuse a pharmaceutical or biotechnology company with a software company, but the level of technology used in clinical trials makes a strong argument that the industry is technology-enabled. Some level of IT capacity is needed to support and maintain systems used in conducting clinical trials, but successful implementation must be driven by the business.

Individual implementations of EDC come with a unique set of requirements for integration with coding systems, severe adverse event (SAE) reporting, trial management and grants management systems. These integrations will involve investment in software development for either conversion or "adapter" programs or reports. This will require a level of IT capacity, regardless of whether the system is vendor based or custom developed, and regardless of whether IT is outsourced or in-house. With pharmaceutical and biotechnology companies trending toward outsourcing rather than internalizing IT capabilities, including software development, this capacity is becoming less common internally.

Making the right decision

The most important aspect of ensuring good decisions when debating whether to build or buy an application is having a clear strategy for EDC implementation.

A clear strategy should include looking beyond the initial cost and time of implementation and should consider interfaces to other applications, commitment to industry-standard data definitions and structures such as CDISC or HL7 (the Clinical Data Interchange Standards Consortium and Health Level 7 are data and information standards widely used in the pharmaceutical industry). Other important factors include a careful assessment of your corporate culture, financial and human resources and the number of trials you expect to conduct with EDC.

Successfully implementing EDC can have tremendous financial and efficiency benefits for your company. For some, the choice of building versus buying may be obvious. For most, the decision is still worthy of careful consideration, as there are important expenses and details associated with both approaches. ■

Going Paperless for Clinical Trial Data Collection: Perspective from a Clinical Application Systems Analyst

Jane F. Kuczma,CCDM, Genentech, Inc.

Recent research comparing the use of paper-based trials versus electronic data capture (EDC) methodology continues to show multiple advantages of implementing EDC. Our industry is embracing this new territory in pursuit of expediting and improving the collection, cleaning and analysis of clinical trial data to shorten submission time to the Food and Drug Administration (FDA) and ultimately get our drugs to market sooner for our patients.

This process shift unquestionably affects those who build and program databases. In particular, it focuses greater attention on such elements as standardization, timing, user acceptance testing, user interface and system performance.

Standardization

Without a doubt, the adherence to standards within studies and across projects helps reduce build and programming time when focusing on tight timelines. It is important, as often as possible, to refrain from the temptation of uniqueness for a study and instead to drive changes based on critical business need only. Three reasons for adhering to set standards are:

- Avoidance of build delay due to deviation process
- Reduction of time to modify database objects
- Elimination of the possibility of cross-impacting another part of the system

There are a basic set of data collection modules companies set up to meet FDA expectations as typically outlined in a study protocol. The use of database standards can often be traced back to protocol execution teams' adherence to following set protocol template standardization. Often there are optional fields for certain forms that can be removed if not collected in a study. Deviations from standards may not become obvious until the project data manager begins working on the standard mock electronic CRF (eCRF) template and cross-checking to the protocol. The process of identifying and submitting deviations for approval can delay both finalizing documents and building the study database (which is dependent on the final document).

Once deviations are approved and documents are finalized, the CASA must make necessary changes to the database. The amount of time it takes a CASA to update the standard database objects originally copied into the study can be daunting–so decreasing or eliminating modifications to standards is highly recommended.

There is often a cross impact that results from having to change one seemingly minor database item. Being aware of the cross-impact is a CASA's specialty. While the database update may take only a few minutes, unintended cross-impact issues may involve hours and hours of edit-check revisions.

Why is standardization so extremely important for EDC studies? It's all in the timing.

Timing

In a paper-based environment, the main focus was often on making sure the final set of case report form (CRF) binders were at the site by the time of the first patient in (FPI). A functional (data-entry-ready) database was considered a nicety rather than a necessity, since CRF data could be collected on paper and entered either in-house or at a CRO at a later date. Not having a functional database available for FPI rarely resulted in postponing or delaying the study in the paper-based environment.

The shift of technology to EDC emphasizes the submission of subject data directly into the database rather than on paper CRFs for entry at a later time. The availability of the complete functional database at all sites prior to FPI is now the main driver of study start-up. Not having a functional database available at FPI can contribute directly to postponement or delay of study start-up or FPI. One of the main differences in the EDC world is the new role the CASA assumes by being included as a member on the critical path.

With the clock ticking, it is critical that the database made available to sites is built correctly and functions as expected. One way to ensure a high quality product is to perform robust user acceptance testing.

User acceptance testing

Quality of the build is of utmost importance; having to update a database mid-study due to undetected build errors can have negative impacts on budget, resources and system availability.

User acceptance testing is critical to ensure the database being released at sites is accurate and correct. The screen and help text being used should be detailed and deliberate. Help text should be associated with the proper fields. The order of the fields and actions that result when entering data from one field or form to the next should be predictable and seamless. With all of the sites using the same tool, any error not found and needing correction later can have dramatic impact on the conduct of the trial. User acceptance testing is typically done by a person or group other than the builder. Often, a list is made of the most important parts of the database that should be tested for all studies. User acceptance testing is done for both the database build and edit-check programming.

Any issues found are addressed and fixed either by updating documentation, updating the database or both. One consideration addressed during user acceptance testing is how easily the end user (site coordinator) understands the type and format of data expected to be entered into the system. This leads to

Continued on page 8

Going Paperless for Clinical Trial Data Collection: Perspective from a Clinical Application Systems Analyst

Continued from page 7

another important consideration, setting up a user (friendly) interface.

User interface

Instead of a site pulling a binder and filling out a CRF page by hand, in an EDC scenario the site coordinators rely on data entry screens designed and tested by the sponsor.

In the paper-based world, data entry professionals played a key role inputting the data from paper CRFs; they were well-versed on entering specific study data (often through the use of various tools such as tip sheets). By shifting the data entry responsibility to site coordinators (often personnel without specific database knowledge), a heavier emphasis is placed on sponsors to create data entry screens that are far more intuitive for the site personnel.

Hard-copy tip sheets for paper-based data entry reference have been replaced by online help. Help needs to be short and concise but detailed enough to guide site coordinators through entering the data correctly into the online system.

Sponsors need to be aware of blind spots that may exist at the site. For example, an instruction to "enter a value for XYZ" may be too vague for a site if they cannot figure out how to determine the value in the first place–especially if there may be more than one method to calculate the value. While this may not directly impact the database build, ultimately the value placed in a field may result in an update needed to the field definition (e.g., a decimal response may be required instead of a whole integer).

The use of instant discrepancy feedback bound to certain fields can cause challenges for sites, from system performance issues to restricting them from bypassing an unknown value to partially complete a form with the information known at that point in time. Entering data for a site in these situations can become a very frustrating endeavor.

The factor that most affects site performance is the reliability and availability of the database system, otherwise known as system performance.

Performance

Reliable system performance is critical for sites to be able to enter clinical data in a fast, efficient manner. Database software often has inherent limitations, subject to review and revision, that may result in system upgrades to help reduce the amount of wait time a site must endure to get all of their data entered.

Other controllable factors that must be addressed to help facilitate peak performance include reducing the complexity and actual number of edit checks that fire. Experienced CASAs often have insight into how to build non-standard forms that help improve system performance and can ultimately help reduce the need for complex custom functions.

It is critical to implement system efficiencies that increase system performance and site compliance and performance.

Proactively working toward greater efficiency through awareness of the impact of various EDC functions such as standardization, timing, user acceptance testing, user interface and performance can greatly reduce timelines, increase quality and ultimately get medicines to market for those countless patients in greatest need. ■

Jane F. Kuczma, CCDM, is a Senior Clinical Application Systems Analyst in Clinical Data Management at Genentech, Inc. In this role, she provides technical support to clinical data management, emphasizing Oracle Clinical and Electronic Data Capture applications. Jane is a member of SCDM, DIA and HBA.

PLEASE NOTE:

SCDM does not sell its membership list and does not condone the use of the on-line membership database for electronic broadcast marketing activities.

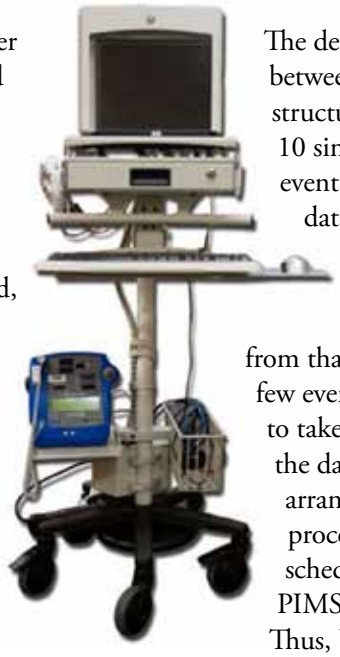
In order to be more environmentally conscious, *Data Basics* will be sent to you via e-mail beginning with the Spring 2009 issue. The publication will still be available in its familiar format. For questions or comments, please contact us at info@scdm.org.

Lynda Hunter,
SCDM Publications Committee Chair

Blazing Through Phase 1

Brian R. Poirier

Is it possible to set up a clinical trials database in under four hours, have immediate access to data on demand during study conduct, close and lock a database 24 hours after last subject last visit with next to 100 percent cleanliness? The answer; yes, it is. How is this done? It is done with two key ingredients. First, start with a user-friendly, malleable application that is tailored to study database design and scheduling. Second, have a global approach to the development of standards, processes and procedures to employ a database tool effectively, to its full potential to achieve various business goals.



The Pfizer New Haven Clinical Research Unit (CRU), which opened its doors in April 2005, is a 50-bed Phase 1 research facility. It is one of three CRUs operated by Pfizer Inc. Establishing a new CRU afforded an opportunity to explore new approaches to handling study conduct and data. The database tool that was chosen for superior data capture, database building and study scheduling/project management was Phase I Management System (PIMS) by RM systems. Most Remote Data Capture (RDC) systems work by forcing a CRF page into an electronic system. PIMS does not do that and is a malleable application that was designed by an individual with over 15 years of Phase 1 research experience. A few highlights of the system's strong points are:

- Incorporates data as it is captured as a source document
- Directly interfaces with collection equipment eliminating the need for paper source documents
- Promotes immediate (24/7) access to collected data
- Builds databases as a "living protocol", which enhances scheduling, project management, data cleaning, and in-line quality assurance
- Decreases the need for data cleaning/data management overhead

The design of the PIMS system allows for an easy flow between a protocol's schedule of activities to build a structured database and data collection tool. There are 10 simple questions to answer for each data collection event. They are set up in a system that allows for easy data collection based on study period, cohort, gender, or treatment regimen component. Events are timed based on a dosing event as time zero with a schedule of activities naturally flowing from that point onward. Immediately after inputting a few events into the system, the study schedule begins to take shape and allows for an easy way to check into the day in the life of a study subject. The "protocol arrangement" nature of the system lends itself to both process and workflow management. A home-grown scheduling system and dashboard interfaces with PIMS and is a personnel scheduler for unit activities. Thus, by building a database, one sets up the shell for employee scheduling for weeks and months to come. Nursing and technical staff can be assigned per protocol or per event that they are trained to cover (AE checks, blood collection, ECG, vital signs, etc.). When a protocol is final in the system, one can view the schedules for both subjects and assigned personnel.

A key contributing factor to the cleanliness of PIMS data is the fact that the system is also the source document. There is no need for any transcribed data. There is minimal manual data entry. Data flows directly from the applications via an electronic interface between the GE DinaMaps used for vital signs collection (blood pressure, heart rate, and temperature), electrocardiogram carts, and the internal laboratory systems. Some of the systems have the ability to flag errant data prior to its transfer to PIMS, which decreases the likelihood of capturing incorrect data points. PIMS also has a built-in two-tiered trigger system that will prompt a user regarding possible errant data. There is an initial alert if there is a data value that is approaching an out of range level; this can be bypassed by hitting the enter

Continued on page 10

Blazing Through Phase 1

Continued from page 9

key. There is also a warning level where the user has to type the word ACCEPT to allow the value to transmit. These alerts are configurable per protocol. With this in-line quality assurance process, we do not need external range edit checks and clean data is nearly 100% assured.

PIMS is driven by barcodes that identify each subject, each piece of equipment, and each study event or blood tube labeled in a protocol. Errors are greatly reduced as the system will not allow a user to scan an incorrect barcode for any of the items without a warning which cannot be overridden. There is no manual data entry involved, timing mechanisms ensure data are captured on-time or it is flagged as late to the user. Data management overhead and the need for endless edit checks are greatly reduced when the data are forced to be captured correctly up front. The error rate has been minimal with about half of our completed studies having 0 errors and half at about 1-2 errors total.

The data system and standards are half of the puzzle. The other half was the effort to develop processes and procedures to maximize the system potential and also to create a cultural mentality of collecting and analyzing clean data. Such a process would not require additional resources and would be efficient, putting no additional burden on the daily workflow. This was done to achieve:

- Quick, easy database builds
- Efficient, effortless data collection, cleaning, and reporting
- Constant data availability
- Database closure and final study reports as soon as possible after LSLV (Last Subject Last Visit)

To engineer the process, a global Systems Governance Team (SGT) was formed which was comprised of key personnel from the CRUs with experience in a variety of experience in informatics technology, data management, statistical analysis, programming, project management, and study management activities. The correct group composition was imperative to ensure that processes were engineered from start-to-finish across all disciplines. We kept our vision global with the goal of strong communication, information sharing, and ultimately choosing best practices from all sites and turning these practices into standards. Committee members interfaced with all of the staff at each CRU (nurses, technicians, physicians, etc.) to ensure that they had a continuous opportunity to provide feedback. This feedback comprised the agendas and become global group troubleshooting forums. Over three years, this has fostered a communication paradigm that is so efficient that it has gone from twice-weekly teleconferences and quarterly face-to-face meetings, to once-weekly teleconferences. This well-oiled machine is a part of the backbone of a culture of continuous improvement that has become a way of life. This team effectively engineered the process across all disciplines.

Global cross-training and information sharing standard default events have been developed in PIMS that allow the builder to copy down events that are common among protocols such as a Screening or Check-In visit. Simpler studies such as bio-equivalence or Absorption/Distribution/Metabolism/Excretion (ADME) studies can be built in about 1 hour. A complex study design may take a day or more, but the more exposure to similar blueprints, the faster the build the second time around. Quality data is built in because the system has a direct interface with collection equipment; and because staff members check the "data cache" or the data collected each shift as a working practice. Clean data are seen as everybody's responsibility from the physician to technician. The staff is trained to call up a screen view of the data they collect and double-check for complete, correct, and consistent data. Thus, at the end of each shift, clean data is readily available through a variety of viewing tools which can be launched from anywhere in the world. If an issue arises it is addressed immediately, not upon a retrospective review.

Project management and nursing staff also keep close tabs on a deviation log that our programming colleagues can access if they see something in the data extract that looks to be askew. If it is documented in the log, it will not need to be queried because it will be accompanied with a reason (i.e. a vital sign was missed). The staff are also well trained in what the data they collect means and how to make it tell a complete story. If they are capturing an AE, they know to think of concomitant medications or treatments as well as any additional collections of data like an additional electrocardiogram (ECG) or vital signs measurement. They also capture detailed progress notes directly in PIMS which can be viewed by any user. This ownership of data that filters down to each employee alleviates the need for extra data management and study management/monitoring staff. The expertise is in the building at every level of employee so that problems can be resolved in real time.

Once the data are in the system, data viewing tools can be used by any user with an account and the proper privileges to access study data. The data review tools sit on top of the application and allow the user to view single study data or to integrate data across studies. This means that clinical teams from the U.S. to Europe to Asia can review draft data earlier to assess risks and make efficacy arguments sooner than with traditional paper case report forms or slower electronic data capture systems. It streamlines safety reviews and Pharmacokinetic (PK) concentration analysis. It also has enhanced pharmacodynamic analyses, PK modeling and rapid review of a variety of other physiological biomarker data. This system gives the team real time deci-

Continued on page 11

Blazing Through Phase 1

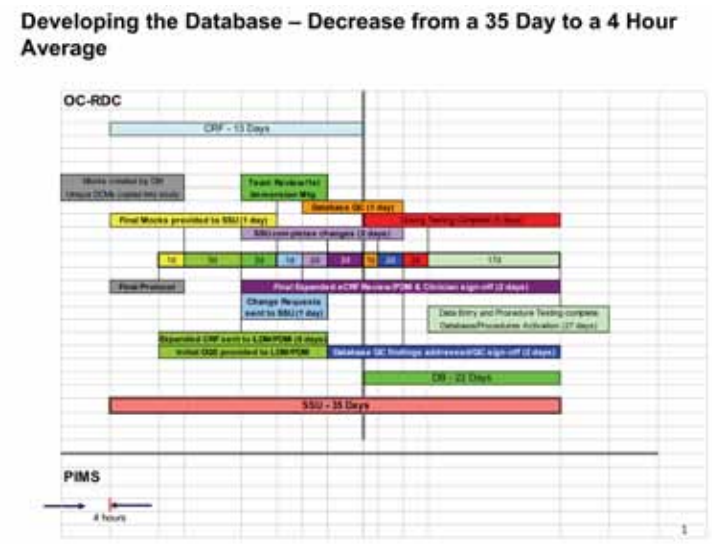
Continued from page 10

sion-making ability which may change the direction of a trial or kill a compound earlier on in development, saving resources. It directly encourages innovation.

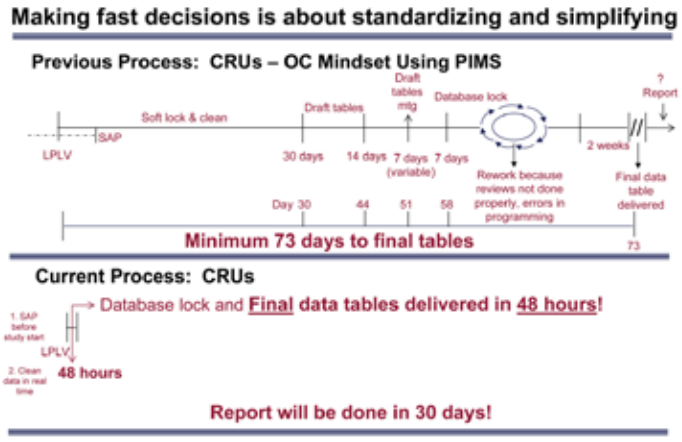
Since data are cleaned daily, in real time, when LSLV occurs, the final subject summary is expected to be signed for medical clearance by the PI within 24 hrs of LSLV. The blind for blinded studies is broken and the database locked. Clinical programming colleagues are keenly aware of study timelines and have created the table and listing shells for the data to be ready for final extraction when the database is locked. They are able to deliver final tables and listings, sometimes immediately and nearly 100% of the time within 24 hrs of database hard lock.

Two of our Greatest Milestones

A decrease in database development time from a 35 day average to approximately four hours



A decrease in final data listings and tables delivered from 73 days to 48 hours



A recent milestone that illustrates the SGT, business processes and PIMS in concert was the evolution of our Lab Review Module (LRM) system. Between the physicians, the laboratory, IT, and project management the business saw the need for the following:

- paperless review of all lab data with complete 21 CFR Part 11 compliance
- tight integration with the screening review module to allow laboratory evaluation to be employed for subject selection – no subject is allowed into a study until every lab value is reviewed
- paperless ordering of repeat/follow-up labs with email notification to internal staff
- tight integration with the labeling and scheduling functions
- fast and easy to use

Pfizer IT first identified the ideal workflow in conjunction with RM Systems and the software was then written, evaluated, tested and accepted. In parallel, a subset of global SGT worked out the internal tactics, processes and procedures for the effective use of the software through multiple testing sessions involving physicians, the lab, and IT staff. This process is was recently deployed and is still evolving and being enhanced, but we have already seen the great benefits of time savings; instant retrieval of historical data; the elimination of all paper in the process (no lost paper lab reports); no lost follow-up lab orders; no risk of a subject accepted into a study with unreviewed data; direct accountability for the scheduling of follow-ups and label printing.

Through disciplined processes and standards, a focus on fine-tuned process engineering, and with the proper tools and individuals who understand what is needed, study conduct can be optimized without any additional resources. The dynamic nature of the business and constant change will dictate which direction this will go. ■

Brian R. Poirier is the PIMS Systems Administrator for the Pfizer Clinical Research Unit in New Haven, Connecticut. He has a Bachelors in Anthropology with a minor in Biochemistry from the University of New Hampshire, Durham, NH and a Masters in Public Health from Boston University. His role includes database setup and study data workflow management from protocol review through reporting final study tables. Brian works closely with in-house colleagues and customers including laboratories, pharmacies, physicians, project managers, clinicians, and drug kineticists.

Effective Clinical Trial Monitoring Using EDC Metrics

A.V. Prabhakar, PhD, Manager, Clinical Data Management, Quintiles

Despite its slow adoption, the use of EDC is on the rise.

"By 2012 the expected number of EDC studies would be greater than 70%."

- By David Handelsman

Background

During the past 20 years, technology has developed to assist electronic capture of clinical trials data. And while electronic data capture (EDC) is not a new concept, it is taking a long time to be widely adopted in the pharmaceutical industry. Consider a few compelling numbers that are associated with the drug development process. The average cost of developing a drug is nearly $1 billion and only three in 10 drugs recover their cost of development. The average number of trials per New Drug Application and the number of subjects has more than doubled over the last decade; subject enrollment deadlines are missed 80 percent of the time and development times have climbed from 33 months to 68 months.

We as an industry need to work smarter to accelerate clinical trials and reduce time to market. EDC is a key component of innovative trial management—applying web-based technologies to enhance trial performance, achieving shorter project timelines and producing cleaner data faster. EDC is not new for the pharmaceutical industry; the technology has been available for many years, through the experience with it has been a mixed reaction among the end users. Although a complete and sudden move to an e-clinical environment can be difficult, gradual implementation of current core technologies can help gain significant efficiencies that can translate into real savings in both time and money.

Pfizer, Bayer and Novartis have been early adopters of the EDC technology. In 2001, Novartis converted data capture from 100 percent paper to 100 percent electronic. Bayer implemented EDC technology in 1989. Pfizer might have saved around $85 million between 1998 and 2003 by implementing EDC technology. The benefits of EDC are widely reported, but very little is known about how the metrics can be effectively used in global studies for assessing the monitoring processes.

An attempt is made in this paper to understand the use of standard metrics obtained using Adhoc Reporting tool of Inform to track and improve upon the clinical monitoring process.

Advantages of EDC over paper data collection

There are various advantages of EDC over paper:

- Elimination of in-house data entry
- No expenses for printing, distribution and filing of CRFs
- Decrease in time from last patient visit to database lock from six to 12 weeks to around two to three weeks
- Can be current on day-to-day basis with regards to discrepancy management
- Access to real time data at any given point in time, enabling timely decisions regarding continuing or discontinuing the study
- The study-related metrics such as Data Entry Lag, Query Aging, Queries Open, Queries Reissued, etc., can be easily obtained for EDC studies from the system and the same information could be shared with the clinical monitoring team which enables them to perform their monitoring better
- Startup activities for EDC study are minimal as compared to paper study thus an early go live
- Immediate detection of transcription errors results in fewer queries
- Real-time edit checks can be fired to alert for missing and inconsistent data. These edit checks save time, money and improve quality of the data compared to paper based clinical data management systems
- Costs for query management are reduced, as there is a marked reduction in the number of queries as well as the time that it takes to resolve a query
- No physical storage space is required for storage or long-term archival of case report forms
- More positive image with the trial investigators.
- Better resource management
- Direct access of data for regulators

Current trend of EDC in life science

Life sciences companies globally are turning to e-clinical solutions in an attempt to cut down costs during clinical trials. On average, life science companies spend between $12 million and $17 million yearly on mailings and copies of paper case report forms. With the implementation of eClinical solutions, a company could save anywhere from $10 million to $15 million a year on paper and postage alone.

Organizations are increasingly turning to CROs and other service providers to manage all or parts of their clinical development process. Fueling this growth in outsourcing is the increasing complexity and growing size of studies, as well as the trend to conduct clinical research globally.

Companies are, however, beginning to recognize the value in using EDC, and industry conferences showcase a wide variety of EDC products from vendors such as Phase Forward, Medidata, DATATRAK and e-Trials to name a few.

Knowing the potential benefits of EDC has led most life sciences companies to pilot or adopt an EDC program. Many of these companies that have used EDC realize there is no going back to paper. A number of them aren't quite ready to completely abandon their paper-based systems – since that would require not only

Continued on page 13

Continued from page 12

new technologies but new business processes as well. Without changing business processes to leverage new electronic systems, the true potential of EDC systems is unlikely to be realized.

Additionally, the growing adoption of the Clinical Data Interchange Standards Consortium (CDISC) standards is driving the effort to have the life sciences industries adopt a common data collection format. This common format can significantly ease the burden both on investigators and research companies. The CDISC data standards and data models can be applied to the design of data capture screens so that EDC interfaces are similar across products. At a broader level, the protocol representation group within CDISC is determining ways to define the protocol, or the rules of conduct for the research trial, in XML so that data-related activities associated with a clinical trial can be defined in the same context as the rules. Doing so will further expedite – and perhaps even automate – data collection, management and analysis.

EDC metrics availability

The shift from paper to EDC is still too fresh to gauge quantifiable metrics or facts.There is not much literature or many published papers available on EDC metrics. This paper is expected to help clinical trial monitors to know and understand the metrics which would aid them in carrying out effective trial monitoring.

What are metrics and how EDC metrics can increase clinical efficiency?

Metrics are typically used to monitor productivity and ensure that the process is operating as intended or to ensure that the resources are properly allocated. It is also important to make an estimate and to have a real time clear visibility of all end points in order to achieve the primary objective.

The metrics will help us know the efficiency and turn-around time of clinical trial monitors and sites. The metrics information provided to clinical trial monitors/sites on a weekly or monthly basis will help them know:

- Efficiency on a particular study
- Turn-around time for resolving queries
- Backlog status (e.g. numbers of queries in open status, pending signatures, forms pending for locking and freezing, etc.)
- When to plan monitoring visits

Based on these metrics, clinical staff can add efficiency to their monitoring visits to ensure that they have better turn-around time and no backlog as they near the critical milestone of database lock. In this way, we can assist monitors to be more efficient in getting their site data verified.

Different types of EDC metrics

Here are a few key EDC metrics which can be shared with study trial monitors on a periodic basis (e.g. weekly, monthly) that may have a significant impact on the clinical monitoring and result in a smooth and earlier database lock.

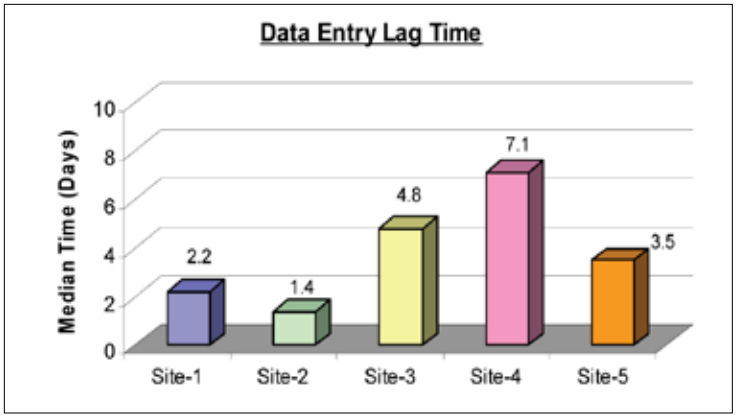
Metrics	Definition
Data Entry Lag	Data entry lag time per site (Difference between Visit Date and form started, in days) per site.
SDV Lag	SDV lag time per site(Difference between Form complete to SDV Complete in days) for each site
Queries Open Answered Lag	Query open–answered lag time (in days) for each site
Queries Open Closed Lag	Query open–closed lag time (in days) for each site
CRF Started to Completed	Difference between “start of form” and “completion of form” (in days) for each site
CRF Complete to SDV Complete	Difference between “date of form completed” and “date of form SDV completed” (in days) for each site
CRF SDV Complete to Frozen	Difference between date of completion of “SDV form completed” and “date of freezing” (in days) for each site
CRF Complete to Frozen	Difference between date of form completed and date of freezing (in days) for each site
CRF Frozen to Signed	Difference between date of form frozen and date of signature (in days) for each site
Queries Open	Number of open queries
Queries Reissued	Number of reissued queries
Query Aging	How old is the query in open status
CRB (Case Record Book) Status	Percent of CRBs that are clean and w / query

Continued on page 14

Effective Clinical Trial Monitoring Using EDC Metrics

Continued from page 13

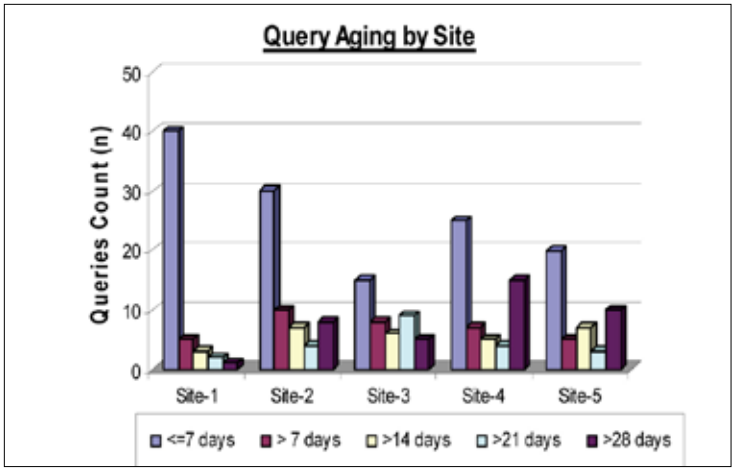
Note: Diagramatic representation of some of the key metrics is provided below.



This metric will give us the lag time (difference between DOV and form started).

The higher the data entry lag time (median days), the poorer the efficiency of the site while the lower the data entry lag time (i.e. median days), the more efficient the site.

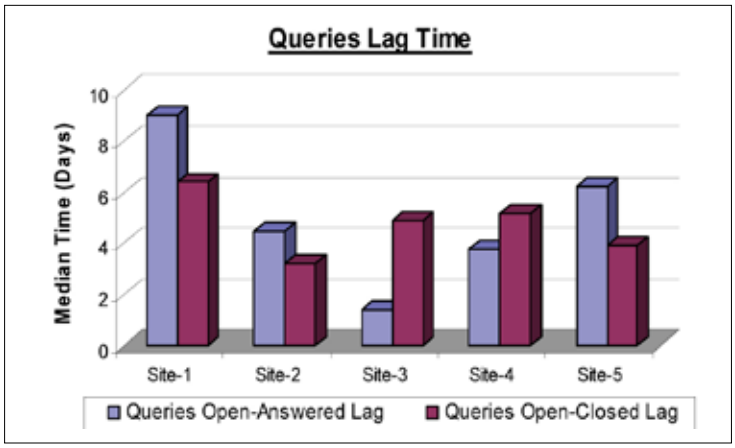
As can be seen in the graph site No. 4 has median data entry lag time of 7.1 days which is very poor as compared to site No. 2 which is very efficient as it has the data entry lag time of 1.4 days.



This metric will give us the number of days the queries are in open status and it is stratified by site.

As can be seen in the graph Sites No. 4 and No. 5 have higher number of queries which are in open status greater than 28 days.

The site monitor' for these two sites could be followed up for the pending status of query for so many days.

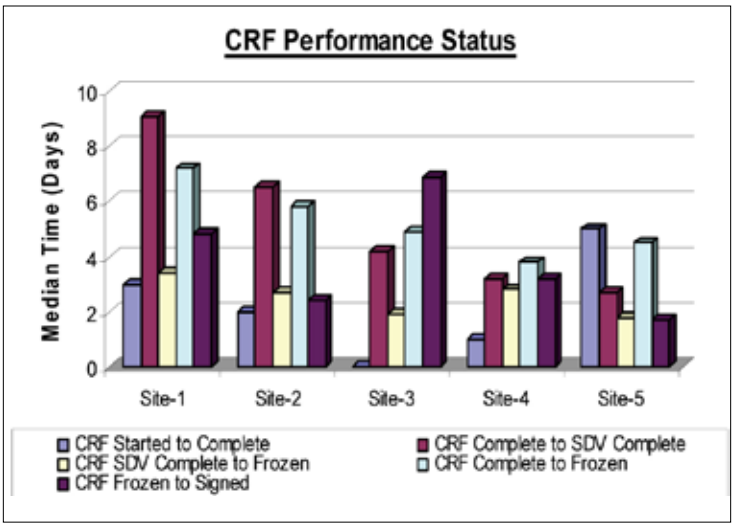


This metric will give us the lag time of open-answered query and open-closed query.

As can be seen in the graph Sites No. 1 and No. 5 have high lag time (Median Days) for open-answered queries.

Higher lag time for open-answered queries indicates clinical inefficiency. The monitor of site could be questioned for high lag time of open-answered queries.

Open-Closed lag time indicates the overall life of a query.



This metric will let us know the performance of study monitors.

High median time (days) for CRF complete to SDV complete necessitates relooking at the monitoring visits.

Conclusion

In recent years with the advancement of EDC technology there has been significant improvement in the area of clinical data management. The EDC metrics discussed in this paper would

Continued on page 17

The Multiple Cohort Study Design and Supporting Discrete Reporting Milestones

Arthur R. Shaw and Eve Pickering

As industries constrict due to the changes in the economic climate, the common adage I think we all hear is "do more with less." My feeling is that it has been extensively noted in the development of pharmaceuticals. One of the unique opportunities that has emerged in an effort to save costs is the multiple cohort study design (MCSD). It is a form of adaptive trial design where the protocol is drafted to cover multiple study types of protocols. The good news for this design is that it enables the development team to move quickly through several study designs within one comprehensive study. The challenges it poses to the data management team are pretty extensive. However, a strong partnership among the clinical colleagues, project management and the operations team members could lead to new opportunities and efficiencies. This article will focus on the example of phase I and II studies in oncology.

Cost and time savings that justify such an approach

Historically, most studies in Phase I are discrete studies. The protocols would either detail dose finding, drug-drug interaction or proof mechanism pharmacodynamic marker studies. These studies would only address one of the distinct designs noted above and, as a result, their format was generally very straight forward. They were carried out with healthy subjects a majority of the time.

The only efficacy information usually discerned from such a protocol was possibly the establishment of a pharmacodynamic marker that related reliably to the drug under study. This study format allowed for the completion of a study quickly, generally one to three months. This enabled quick turn around and timely updates to regulatory bodies and internal strategy teams as well.

Roll-out of oncology compounds and cost constraints

The treatment of cancer generally involves medications that cannot be provided to healthy subjects, as they would make them extremely ill. As a result, the start-up costs for oncology trials are quite high versus a traditional phase I study. They also require significant discussions with the hospital sites, extra funding and logistics for traditional and some times exotic safety/efficacy laboratory assays, and imaging analyses required to monitor the progress of the treatment. In addition, most subjects are continued on the standard of care treatment (and whenever possible the drug under study) in order to establish exploratory information on how the drug will influence survival.

As a result, clinical teams will take advantage of MCSDs to execute the study in a more timely fashion with less start up costs incurred. An example of an MCSD is a phase I sequentially designed dose finding followed by a drug-drug interaction cohort study. This, on paper, would halve the start-up costs and significantly reduce the negotiation timelines with the sites running the trial, provided that the sites are very savvy in executing such a trial and the tools and resources are deployed which will allow for success.

More recently, study teams have embraced the philosophy of obtaining multiple types of information by running sequential or overlapping cohorts under a single protocol number, thus compressing timelines further. Most therapeutic areas can benefit from this approach. Oncology teams were among the first to adopt this strategy, and there it has become the norm.

Tools for success

The data manager (DM) really needs to be involved in the strategic discussion where the entire phase I development plan is laid out. They do not need to understand all the details of the science, statistical designs and dosing strategies. They do need to understand the general design of a trial and its impact on the case report form (CRF). They also need to know how to plan for risks well in advance of a requested change. The pivotal attribute for the DM is that they should be able to integrate their thoughts and vision into the study team in a helpful and polite manner.

In the circumstance of a multiple cohort study the data manager must be able to synthesize a lot of information and provide direction in a clear and meaningful way. They need to oversee the build of the database and impart knowledge to the database builders. Effective data management communication can be demonstrated by providing the database builders enough details such that they can design the database independent of the flow diagrams within the protocol. As a statistician noted to me, "*A flowchart is not the big picture. It is the trees, not the forest.*" This is particularly true with adaptive studies such as the MCSD.

You cannot assume it is correct because it looks just like the flowchart. Who hasn't deviated from a flowchart?

In addition, the data manager must adapt to take advantage of all new information noted for the compound. If the CRF risk analysis was carried out correctly the team should be allowed to insert a page into a casebook with ease for the subsequent cohort or to remedy a current data collection issue. For example, let's say your DDI cohort requires triplicate ECG collections. The subsequent ECG pages should be, for the most part, formatted the same as the original single ECG data collected in the dose finding cohort of the MCSD. It is also possible that the design of a particular cohort will depend on results from a previous cohort. Even in this case of a (Bayesian) adaptive design, it should be clear during protocol development what the possibilities for each cohort will be, and basic decision rules will be outlined.

If you find that your business unit lacks the standard formats or technology to change a collection module to suit such a design you may want to initiate a standards group. The content of the

Continued on page 16

Continued from page 15

group should be individuals from every discipline that supports the protocol as well technology professionals well-versed in CRF design and electronic data loading.

Protocol

The protocol must be carefully written to address the scientific design of both studies. The author must have a real eye for detail and an in-depth understanding of all aspects of cohorts defined. Generally, a tremendous amount of input should be included from the statistician as they are often a bridge between the clinician's ideas and what can be tangibly collected within a trial. If these items are clear then it will ensure an accurate risk analysis from the data manager and ease of reporting for the statistical programming team.

All amendments should serve only to clarify the original protocol. If there is a significant redesign of the second cohort that would cause a last-minute ground-up rebuild of the database this could be disasterous to the data management team. In addition, there is a good chance that such an undertaking will not have undergone the original scientific rigor of the initial protocol. Your only response to this request is to objectively note the risks and carefully partner with the database builders to get a good database product returned to the team.

Good partnerships with site and project management colleagues

If you have a well written protocol and functionally sound database the trial could post enormous successes provided there is a close collaboration with the site and project/vendor management folks. If the data can be collected in real time, cleaned and locked then potentially the study could be reported out in the cohorts in a sequential manner.

For example, the study described above would look like the figure below (though grossly simplified).

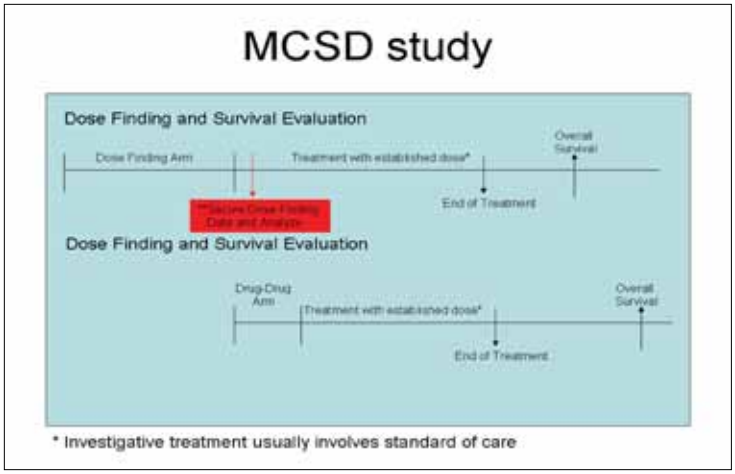
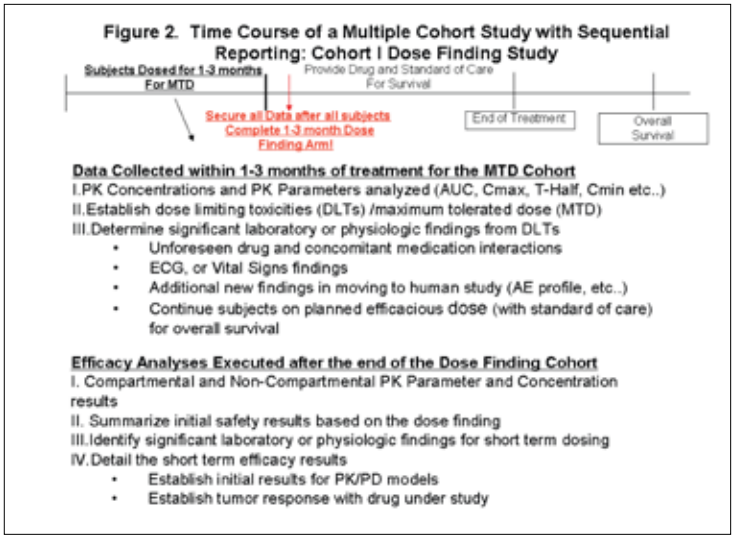


Figure 1. Timeline of multiple cohort study design: Dose finding followed by drug-drug interaction protocol

Please note that the dose finding arm of the study is completed well before the end of the ongoing trial. Therefore, careful planning with the site management team could allow for completing the analyses consistent with a traditional dose finding study. Figure 2 notes several possible analyses one could complete in a dose finding study.



The crux of these early analyses would be dependent on retrieving the pharmacokinetic concentration data from the sites for analysis. Therefore, the data earmarked for developing the parameter information detailing the dose finding arm of the study would be loaded independently from the pharmacokinetic concentration assays supporting the drug-drug interaction cohorts. This is where a strong partnership with the site manager and project/vendor management colleagues is essential.

The site manager must ensure that all visits that support the dose finding arm of the trial have been completed by the sites. While data management must ensure that the visits surrounding the above noted information is queried and sufficient quality for reporting. It takes a shrewd data manager to move from the locking of visits to support the close out of an entire protocol versus locking the visits to support a specific subevent that has occurred within a protocol. The site manager and data manager will have to manage expectations with the team as well. For example, how do you report out AEs that have not resolved at this point in time? My suggestion to you is to restrict the tables presented to those in which you may draw a complete conclusion on from the locked visits. Other tables may be presented but careful consideration should be noted on the conclusions you can draw.

Project/Vendor managers must be engaged for the purposes of bringing in the pharmacokinetic concentration data early. Ex-

Continued on page 17

The Multiple Cohort Study Design and Supporting Discrete Reporting Milestones

Continued from page 16

amples of the items they will need to secure from management is additional funding and commitments from the laboratories to provide additional logistics support. Both of these examples increase the costs of the trial. However, the possibility of speeding the end game activities is a key to a successful early stage study. The faster formal conclusions are drawn the more concise planning that can occur for a phase III trial.

Technology and SOPs

Most databases can lock down to the visit level. However, you must have carefully written SOPs in place to take on sub-analyses in an ongoing study. The most pressing issue for data management is that the SOP must in particular define a commitment of the clinical team, and the operations organization to leave the data locked. This will be your most difficult task. As the teams collect further information from the ongoing MCSD they may have the tendency to say "maybe that isn't quite what it should be….we should open that visit up and query."

Opening up a visit really creates significant issues to the clinical programming team. Tables will have to be rerun and standard quality control checks will need to be regenerated. In addition, the statistician and clinical study report writer will have to revise their conclusions.

As a data manager, it is your responsibility to note risks when teams start to "creep" back into locked data. Your best ali in this circumstance is the statistician and clinical programmer. Sit with them and discuss your concerns. If you have in place SOPs that protect your position as a gatekeeper and the support of the statistician and programmer you may avoid costly biometrics overruns. ■

Effective Clinical Trial Monitoring Using EDC Metrics

Continued from page 14

help pharmaceutical companies and clinical trial monitors to evaluate the health status of their projects and operational efficiencies on the study which could lead to better planning of monitoring visits.

Acknowledgement

I would like to thank Arshad Mohammed, Associate Director – Clinical Data Management, Quintiles India for taking out time of his busy schedule in reviewing the paper and providing valuable inputs and suggestions. ■

References

1. *John S.Klein and Laurie A. Kenvin. Using EDC to Improve Monitoring Practices Worldwide.*
2. *Cristina Anselmi, Cros NT. Data Management Metrics – How to use our Instruments.*
3. *Datamonitor. The paperless clinical trial: closer than you think.*
4. *Jules T. Mitchel, Yong Joong Kim, Joonhyuk Choi, Vanessa Hays, Jens Langendorf, Silvana Cappi. Impact of IBCTs on Clinical Trial Efficiency.*
5. *Sriram V - EDC in clinical trials – Imperative or Not?*
6. *Lisa Henderson - Adventures in Web EDC.*

SMITH HANLEY

an inVentiv health company

Recruitment Specialists since 1980

Clinical Trial/Research Coordinators

Clinical Research Associates

Clinical Project/Study Managers

Clinical Scientists

QA/QC Auditors

Medical Monitors

BRIDGING TALENT & OPPORTUNITY

Contract Staffing:
Bonnie Knowles 800-684-9921
bknowles@smithhanley.com
www.smithhanleyconsulting.com

Permanent Placement:
Jean Kim 800-989-5627
jkim@smithhanley.com
www.smithhanley.com

an inVentiv health company

Data Basics

Submission Requirements

Editorial Board

(also known as Publications TaskForce)

Chandra Wooten, TaskForce Leader
Gilead Sciences, Inc.
206.832.2016 •
chandra.wooten@gilead.com

Rehana Blunt
Clinimetrics
805.499.9295 • rblunt@clinimetrics.com

Kyle Hart, CCDM
RS Medical
360.882.2407• kyle@gurple.com

Kit Howard, MS, CCDM
Kestrel Consultants, Inc.
734.576.3031 •
kit@kestrelconsultants.com

Lynda L. Hunter, CCDM
PRA International
913.410.2065 • hunterlynda@praintl.com

Tina Lewis, CCDM
Quintiles Transnational
913.708.6600 • tina.lewis@quintiles.com

Frank McDonald
Genentech, Inc.
650.467.7091 •
mcdonald.francis@gene.com

Michelle Meany
Schering-Plough Research Institute
908.740.7471 •
michelle.meany@spcorp.com

Jon Milton
Pfizer Global Research and Development
44.0.1304.645788 • jon.milton@pfizer.com

Derek C. Perrin, CCDM
Pfizer Global Research and Development
860.732.2720 • derek.perrin@pfizer.com

Arthur R. Shaw, CCDM
Pfizer, Inc.
860.732.1383 • arthur.r.shaw@pfizer.com

Janet Welsh, CCDM
Boehringer-Ingelheim
203.791.6164 •
janet.welsh@boehringer-ingelheim.com

Sharon Woolcott
Gilead Sciences, Inc.
206.728.5090 •
sharon.woolcott@gilead.com

Sue Abrahms
Society for Clinical Data Management
414.226.0362 • sabrahms@scdm.org

Publication Policy

We welcome submission of materials for publication in *Data Basics*. Materials should preferably be submitted in electronic form (MS Word). Acceptance of materials for publication will be at the sole discretion of the Editorial Board. The decision will be based primarily upon professional merit and suitability. Publication may be edited at the discretion of the Editorial Board.

Neither SCDM nor the Data Basics Editorial Board endorse any commercial vendors or systems mentioned or discussed in any materials published in *Data Basics*.

Advertising Policy

AD RATES**	x1	x2	x3	x4
FULL Page	$1,064 each	$1,008 each ($2,016)	$960 each ($2,880)	$906 each ($3,624)
HALF Page	$740 each	$700 each ($1,400)	$670 each ($2,010)	$630 each ($2,520)
QTR Page	$450 each	$425 each ($850)	$402 each ($1,206)	$378 each ($1,512)

**Ads are net, non-commissionable.

Advertisers purchasing multiple ad packages will have the option of placing those ads anytime within the 12-month period following receipt of payment by SCDM.

Quarter Page = (3 5/8 inches x 4 7/8 inches)

Half Page-vertical = (3 5/8 inches x 10 inches)

Half Page-horizontal = (7 ½ inches x 4 7/8 inches)

Full page = (7 ½ inches x 10 inches)

MECHANICAL REQUIREMENTS: Do not send logo/photos/images from word processing software, presentation software or Web sites. Files should be saved in the native application/file format in which they were created at a resolution of 300 dpi or higher. Acceptable file formats include AI, EPS and high resolution PSD, JPEG, TIF and PDF.

PAYMENT: Payment must be received with advertisement. Space reservations cannot be made by telephone. There is NO agency discount. All ads must be paid in full.

CANCELLATIONS: Cancellations or changes in advertising requests by the advertiser or its agency five days or later after the submission deadline will not be accepted.

GENERAL INFORMATION: All ads must be pre-paid. Publisher is not liable for advertisement printed from faulty ad materials. Advertiser agrees to hold SCDM harmless from any and all claims or suits arising out of publication on any advertising. SCDM assumes no liability, including but not limited to compensatory or consequential damages, for any errors or omissions in connection with any ad. SCDM does not guarantee placement in specific locations or in a given issue. SCDM reserves the right to refuse or pull ads for space or content.

Please submit all forms, artwork, and payments to:

Society for Clinical Data Management, Inc.
555 E. Wells St., Suite 1100
Milwaukee, WI 53202

Phone: 1.414.226.0362
Fax: 1.414.276.3349
E-mail: info@scdm.org
Web site: www.scdm.org