President’s Message

The temperature may be cooling down, but things continue to heat up with ISPE CaSA. The year has begun in full force with multi-state activity. We have held two Therapeutic Thursdays in the Triangle and one in Georgia. For those that may not have noticed, we have held two successful Therapeutic Thursday in the Atlanta area. If you are not familiar, these events are casual networking opportunities created to bring together like-minded groups to share our professional knowledge and to build relationships on a deeper level.

Our first educational event, brought to you by the Young Professionals, was presented to a SOLD OUT crowd; the Monoclonal Antibody Symposium held at Biogen Idec was a success! Thank you to all that participated in planning, executing and attending.

As we look forward, there are some exciting events you will not want to miss. Listening to you, our Members, we are continuing to create combined events around the end of the workday, so you are able to stop by between the busy work day and the start of family activities.

The first Jane Brown Scholarship will be presented, by Jane, at Oktoberfest on Thursday, October 30. This event, starts at 5:30pm at Koka Booth Amphitheater in Cary, is one you will not want to miss. We have revamped our annual planning session where the committees give you a glimpse of what they are doing into an interactive, networking event with Oktoberfest-inspired food selections, beer pairings from Big Boss and Carolina Brewery, and live music by Old Habits. Instead of power point presentations, committees will have carnival games, corn hole and I have heard rumors of apple bobbing to entice you to learn more.

In collaboration with the ISPE Training November 17-20 at the North Raleigh Hilton, the CaSA Chapter is sponsoring Therapeutic Monday to provide a connection for networking with industry Members that may attending the training event from out of the area. Come by and check it out!

This year’s Toys for Tots event has moved to a new time in combination with the Automation Forum on December 3 in RTP.

To keep up with the latest happenings, make sure you check out the weekly e-blasts that come out each Tuesday morning, or check out the website www.ispe-casa.org. For those engaged in social media, you can follow us on Facebook, Twitter, Linked In or Google+.
Thank you to all of the volunteer leaders that are providing the time to make our Chapter thrive. We are always looking for volunteers; consider how you may get engaged.

If you have not already done so, sign up for Oktoberfest, TODAY!

Heather Denny
President, ISPE CaSA Chapter
Membership Corner

DISCOUNT NOW AVAILABLE FOR NEW INDUSTRY MEMBERSHIPS!
By Terence Morrison, P.E., LEED AP BD+C, ISA 84 SFS

$40 DISCOUNT NOW AVAILABLE FOR NEW INDUSTRY MEMBERSHIPS! Applications can be found online at www.ispe.org/join. Click Join Now under Industry Membership, and enter CASA2014 in the promotion code box. Please remember ISPE’s Refer-A-Friend Program! Earn one free month of membership for every friend you refer. All the details are available at the following link: http://www.ispe.org/membership-referral-program

This discount is not applicable to Students, Young Professionals, Academics, and Regulatory Authority / Government as these all hold discounted memberships already. If you have any question about ISPE or the CaSA Chapter, please contact me at membership@ispecasa.org.

Welcome New Members
New Members who joined July 28, 2014 through October 6, 2014

Frank Loethen
Edward L. Dawson, Jr.
Kelion R. McCall
Randy Thrasher
Robert Dean Landers
Kristine Baldovino
Henry L. Darnell
Delaney K. Kolich
Mariam S. Toma
Nilofar Bachubhai Gogda
Teresa Grace Willard
Adarsh Reddy Rondla
Jennifer L. Kilpatrick
Gregory S. Bailey, Jr.
Lionel J. Randolph, Jr.
Gayle Pasik
Jack Trefftzs
Amber Johnson
Kenzie Koehn
Alexandra Clyde
Tiffany T. Nguyen
BroDerrick C. Nelson
Jamie W. Moore
Rickey Livingston
Saad Rahimuddin
Allison L. Tokarski
Alisha M. Jones
Anita H. DeSantis
Ariana N. Peterson
Brittany K. Nixon
Brittany T. Williams
Carri C. Murphy
De’Ajree T. Branch

Jessica S. Pearson
Najeric S. McMillian
Pooja Potluri
Remayja B. Fields-Dunn
Roseanne Amimo
Shakia C. Watson
Sylvie L. Tshimanga
Winifred O. Okunlola
Curron D. Hill
Jennifer Kim
Alexander K. Nguyen
Jeffrey Adam Clegg
Zhixiang Feng
Johnny W. Lemons
Hannah M. Jester
Taylor L. Kern
Robert L. Lewis, Jr.
Jennifer Ahearn
Alfreda Cooke
Eric Page
Christopher Roth Riley
John C. Matos
Swapna Deepthi Lakkaraju
James Geist
Gregory S. Rood
Elizabeth Dustin
O’Neal Campbell
Susan E. Kaple
Willie Green-Aldridge
Dr. Greg Gibb
Ana M. McClanahan
David Yarley
Mark Pergerson
Mike Morgan
Gwendolyn Wall
Joanne Huang
Kristina Burgess
Bruce Bartlett
Chad Merewether
Andrea Ruosi
Ruby Bost
Jungo Ogihara
Martin Noble
Martin Noble
Andrew M. Lim
Ron Casey
Chastity Long
Amitabh Sehgal
Jacob Andrew Smith
Emma Besaw
Joseph Aaron
John T. Foster
Kelsey Boykin
Brian Harrison
Robert Martin
Jason P. Wyrick
Jordan N. Hjelmquist
David J. Kistner
Wade Dickens
Keith A. Lunday
Christopher Cummings
Patrick O’Keefe
Erik Georges
Robert Lambert
Mark Matis
Christopher P. Smith
22nd Annual ISPE-CASA Technology Conference

By Mike Putnam, Committee Chair

If you attended the 2014 ISPE CaSA Technology Conference, you were part of a monumental day in the life of our Chapter. Feedback from attendees and exhibitors affirmed the event to be the most meaningful and productive in the 21 year history of the conference. Participation of global drug and device manufacturers, educational sessions from industry leaders, and impactful charitable support were among a few features that made the 2014 Technology Conference the place to be for professionals in the Life Sciences community! From the time the conference was held in April, the planning committee has continued their efforts to make 2015 even better. We encourage exhibitors and attendees to mark your calendars as next year will be here before you know it! Here are a few quick facts to know about the 2015 conference.

- 22nd Annual Technology Conference date has been set for Tuesday, March 10, 2015
- Hosted at the Raleigh Convention Center
- Exhibitor Registration opens Tuesday, November 11, 2014
- Attendee Registration opens Tuesday, December 9, 2014

Please look for more details about the Technology Conference in future newsletters as we will spotlight key features and information in each issue. Also, if you would like to be part of the planning committee, please contact me. We have many opportunities for you to help us build the 22nd Annual Technology Conference. Thanks and I’ll see you soon!

Technology Corner

Extensive technical expertise in regulated environments

- Enhance quality & compliance
- Reduce risk & cost
- Increase productivity & equipment up time

877-724-2257 • www.pci-llc.com

BOARD OF DIRECTORS 2014-2015

Committee Chairs
LeAnna Pearson, Student Affairs
Jim Hubbard, Education
John Marr, Networking
Terence Morrison, Membership Development
Jamie Sigmon, Young Professionals
David Smith, BioFest Committee
Mike Putnam, Technology Conference
Rich Stanfield, Newsletter

Officers
Heather Denny, President
Lisa Kerner, Vice President
Bruce Craven, Treasurer
Wendy Haines, Secretary
Matt Gilson, Past President

Directors
Ben Hund
Chip Chappell
Ken Ewan

SEQUENCE
Quality and Compliance Services

toll free 855.844.7171
phone 919.844.7171
fax 253.736.8446
2500 Gateway Center Blvd., Suite 850
Morrisville, NC 27560

info@sequenceqcs.com
CaSA Member Spotlight: Eric Mayer

By ISPE CaSA Newsletter Committee

Q: What is your full name?
A: Eric Vincent Mayer

Q: Birth Place?
A: Vicenza, Italy  (my father was in the Army and we were stationed there)

Q: College?
A: United States Military Academy – Civil Engineering Lehigh University – MBA

Q: Tell me a little about your personal life.
A: I am married to Nancy and have three children – Ian, Stephanie, and Alex. Alex, our youngest and the last in college, is graduating next spring – an upcoming raise for the Mayer family - finally! Our family has been in North Carolina for over 20 years so I guess this is home. I enjoy fishing, golf, and exercise.

Q: What is your present position? What do you do at your job?
A: Manager of Business Development for Avid Solutions. I am part of the senior management team and my role is to secure new clients, maintain relationships with existing accounts and I participate in marketing and business planning for the organization.

Q: How long have you been with your current employer?
A: I have been with Avid Solutions, a process control system integrator, for 12 ½ years.

Q: Tell me about your career path, and how you ended up where you are today.
A: Graduating from West Point, the first five years of my career were in the Army assigned as an officer in the Corps of Engineers. I then moved on to Air Products and Chemicals as a project engineer building cryogenic gas plants. This was my first exposure to process control. After five years there my wife and I decided to move to North Carolina and I ended up securing a job at a process controls company that I used to hire on my projects at Air Products. I then moved over to Avid Solutions in 2002. In addition to sales positions for automation companies I also had some brief experience in sales for general contracting and IT products.

Q: What is your favorite part of your job?
A: Meeting new customers and visiting new manufacturing plants. Walking down jobs and developing ways to solve the customer needs regarding their control systems and automation. Every opportunity is a different challenge.

Q: How long have you been a Member of ISPE/when did you first join ISPE?
A: I originally joined ISPE in the mid 90’s. I may have missed a
year or two while working in the IT industry, but rejoined when I started with Avid Solutions.

Q: What benefits have you realized from being a Member of ISPE?
A: When I think of ISPE-CaSA, I think of the people. I have made some great friends through this organization. Obviously the networking is very helpful from a business perspective in order to understand what is going on in community, but the personal relationships have been much more helpful and rewarding to me.

Q: Why are you still involved with ISPE?
A: I feel it is important to volunteer and give back to the community. I want the organization to succeed and provide benefits to other new and younger Members beginning in their careers.

Q: Any Mentors/Role Models that have helped to shape your life?
A: Probably my Battalion Commander in the Army. He was a great leader, very intelligent, and also a good friend. He gave me excellent advice always, even after I was out of the service.

Q: If you weren’t involved in pharma/biotech, what business do you think you’d be in?
A: I would still be in a technical services firm of some sort. I enjoy engineering and construction because every project is different and presents its own set of challenges.

Q: What is one skill you wish you had that you don’t?
A: The ability to continue growing hair on my head.

Q: Any hobbies? What are they?
A: I like golf and fishing, but my favorite hobby is to go traveling with my lovely wife.

Q: Do you collect anything?
A: Not really. Nancy’s Starbucks coffee cup collection takes up most of the vacant space in the house, anyway.

Q: Finish this sentence – “I need more...”
A: ...purchase orders and ice cream.

Q: Favorite Food?
A: See question above.

Q: What is something that people would be surprised to learn about you?
A: I went sky diving one time and my chute did not open. My tandem partner had to bring us in on the reserve chute. Haven’t been back since, by the way.

Q: Last movie you saw?
A: Gone Girl

Q: For those in the early stage of their careers, what advice would you give them?
A: Seek to develop and maintain relationships with others. Always strive to help your fellow man even if you do not know them very well – that is one way to get to know them. The Life Sciences community is a very small world in the southeast so your personal reputation and integrity are keys to success in your career.

---

**CaSA COMMITTEES 2014-2015**

**Student Affairs**
LeAnna Pearson
ispeCaSAsac@gmail.com

**Education**
Jim Hubbard
jhubbard@amts.com

**Networking**
John Marr
John.marr@crbusa.com

**Membership Development**
Terence Morrison
terence.morrison@crbusa.com

**Young Professionals**
Jamie Sigmon
jamiesigmon@gmail.com

**BioFest Committee**
David Smith,
davidglennsmith@gmail.com

**Technology Conference**
Mike Putnam,
mike_putnam@sequencevalidation.com

**Newsletter**
Rich Stanfield,
rich.stanfield@cagents.com
**Student Corner**

*Exciting News About A Merger*

*By LeAnna Pearson*

The Student Leadership Symposium is MOVING.... We will be integrating with the Technology Conference to be held on March 10, 2014. This is exciting because we can now offer a Student and Young Professional Educational Track!!! We have some great ideas but if you have one, please email us ISPECaSASAC@gmail.com.

This move is in an effort to work with other committees and with the success of the Technology Conference. We could not think of a better pairing! 

---

*Sign Up for Oktoberfest*

*By LeAnna Pearson*

Calling all Schools: Oktoberfest is coming!!! Wear your school colors and come out and represent your student chapter. Ask your local Student Committee for more information or email me ISPECaSASAC@gmail.com to sign up for Oktoberfest. 

---

**ISPE**

*Classroom Training*

*Raleigh, North Carolina*

*17-20 November 2014*

*Hilton North Raleigh/Midtown*
Seeking practical GMP solutions to meet regulatory requirements?

Take ISPE eLearning

NEW EXPANDED COURSES:

- GMP Auditing for the Pharmaceutical Industry
- Biotechnology Basics
- Containment Fundamentals

Plus classic online courses: also science based and given by worldwide experts.

THE DEPTH OF AN IN-PERSON CLASS, ONLINE.

REGISTER TODAY! www.ISPE.org/eLearning
Young Professional Corner

YP Education Event: Monoclonal Antibody Symposium

By Jamie Sigmon

The ISPE Young Professionals hosted a successful Monoclonal Antibodies Symposium September 30, 2014, at Biogen Idec. Subject Matter Experts delivered their presentations to more than 50 ISPE Young Professionals and Members. Dave Clark, Head of Global Technical Operations at MedImmune, began with a presentation on Monoclonal Antibody Basics; Bill Welsh, Process Transfer Leader of Manufacturing Sciences at Biogen Idec, spoke on Process Controls for mAbs; and Shannon Holmes, Senior Manager of Regulatory Affairs at Biogen Idec, wrapped up with a presentation about Regulatory Considerations for mAb Production. The audience and presenters then divided into breakout discussions focused on process and facility design, analytical testing and controls, regulatory and QA considerations, and changeover between products. The opportunities to learn about facility design, process controls and regulatory requirements for monoclonal antibodies, and to network with industry professionals, made for a successful ISPE symposium! We’d like to thank Biogen Idec and the sponsors of the Monoclonal Antibodies Symposium: CRB, Sequence and CAI.
Step up your knowledge with ISPE.

3 Ways to Learn

to increase manufacturing efficiency, maintain product quality, and improve GMP compliance.

- Classroom Training
  Over 50 courses offered at national and international training events.

- E-learning
  Hone your skills at your desk, immediately, with Auditing, Biotechnology, Containment or GAMP® 5 online training courses.

- On-site Training
  Bring ISPE’s expert instructors to your facility for customized training.

New 2014 Training Courses:
- Combination Products
- HVAC
- Process Validation
- Risk-based Facilities, Systems and Equipment

Register Now! www.ISPE.org/Training

A changing regulatory environment requires a guide you can trust.

ProPharma Group
Comprehensive Compliance Solutions
888.242.0559 | propharmagroup.com

Get Involved With Your Affiliate or Chapter Today!

www.ISPE.org/Affiliates-and-Chapters
1 Introduction

It is well understood that each clinical trial is conducted and managed as an independent project even if several trials investigate the same Investigational Medicinal Product (IMP). Each clinical trial is different as each addresses different parts of the development cycle or varying product indications or endpoints. Trial projects, especially across the various phases, vary greatly in terms of duration, number of patients to be recruited, the pace of enrollment, and the spread of geographic location(s) involved.

To address the trial specific setups, eClinical solutions have to be built from various integrated technologies and tools designed to be utilized in clinical trials, working together sharing data, eliminating duplication of activities, and streamlining the use of multiple technologies for the end user (Figure 1.1).

Figure 1.1: Mapping of Sample Systems to the Clinical Process
The need to ensure data integrity through the life cycle of a clinical trial and across all the systems involved is of paramount importance as inconsistent, incorrect or corrupted data could endanger the safety of patients, adversely affect the outcome of the trial and increase the risk of a failure during the submission procedure. Therefore, this aspect has increasingly become the focus of regulatory oversight. One of the main drivers for this has been that the industry has embraced individual or strategic outsourcing of clinical trial activities to Contract Research Organizations (CROs) and sponsors as well as CROs also adopting Software as a Service (SaaS) offerings especially in the area of Electronic Data Capture (EDC) or Interactive Voice Response Systems/Interactive Web Response Systems (IVRS/IWRS). Oftentimes this leads to a chain of partners with an increasing risk of losing direct control for the sponsor. Even when strategically partnered with a CRO, the responsibility to address these risks resides with the Sponsor and cannot be delegated. This requires extensive and increasing efforts for oversight, which must be considered when addressing the risks with regard to data integrity.

While the application of the GAMP® 5 principles to the validation of GCP relevant systems has already been discussed in an ISPE Concept Paper, “The Application of GAMP® 5 to the Implementation and Operation of a GxP Compliant Clinical System,” the challenges in the setup and maintenance of an eClinical Platform are largely not addressed.

2 eClinical Platforms

The introduction of the GAMP® Good Practice Guide: IT Infrastructure Control and Compliance, has also seen the term “platform” officially associated with the IT infrastructure of GxP regulated environments for the first time. A platform provides the technological environment (hardware and software) required for an application to fulfill its intended use. The efficient and quality-assured operation of IT infrastructure is facilitated by the use of reusable building blocks, which consist of logical groupings of standardized system components.

The introduction of GAMP® 5 extended the GAMP® software Category 1 to include infrastructure software (infrastructure software tools and layered software), thereby effectively achieving an interface to IT infrastructure. The so-called “layered software” includes software such as operating systems, table calculation applications or statistical programming tools, which constitutes platforms for the development of applications.

The main difference between this and an eClinical Platform is the fact that the “layered software” focuses on individual software products (instances) in their condition at delivery, while the eClinical Platform constitutes a pre-configured application portfolio as an intermediate layer between the clinical trial process and IT infrastructure.

For the purpose of this paper, an eClinical Platform is defined as a pre-existing environment of integrated computerized systems that can be adapted to support the conduct of a clinical trial by utilizing existing, validated functionality and processes.

Typical platforms include Electronic Data Capture (EDC) system, Clinical Trial Management System (CTMS), electronic Trial Master File (eTMF), statistical systems as well as safety systems and others. Individual components of the eClinical Platform may require set-up or configuration to meet the requirement of the individual clinical trial.

![Figure 2.1: Flow of Information through the Different System Layers](image-url)
To support the collection, analysis and processing of data collected in a clinical trial, highly specialized tools like an EDC system, CTMS or IVRS/IWRS have been developed and have been in use for years. However, today these tools are no longer stand-alone systems as they have been in the past. These systems have become the building blocks of an integrated eClinical Platform that supports the efficient conduct of clinical trials (Figure 2.1).

Not all clinical trials will need all systems being part of such an eClinical Platform (e.g., an open-label trial does not require systems that support blinding of trials). For instance, a Phase I trial may require different systems than a Phase IV trial. A Phase I trial may not require an expensive, complex, multi-lingual and web-based EDC system, as Phase I trials are often conducted in only one location with very few users and subjects. Other examples include a subject recruitment database or a barcode reader that may not be necessary in a Phase IV trial.

Additionally, some systems (e.g., a CTMS) will collect and process data from all clinical trials conducted by the organization without further customization while others (e.g., EDC system) may need to be set up and configured for each individual trial based on the protocol requirements.

A further aspect that needs to be considered is potential outsourcing of activities and the usage of SaaS offerings. The resulting eClinical Platform might span across multiple organizations (e.g., the sponsor of the trial), one or more CROs and SaaS vendors (e.g., for an EDC system) and could even include Electronic Health Records (EHR) systems at the investigator sites.

As mentioned in the introduction, a practical and efficient approach for the validation of GCP relevant systems has already been provided in the ISPE Concept Paper.

A generic example of an eClinical Platform is provided in Figure 2.2.

![Figure 2.2 Example of a generic eClinical Platform](image)

**Definition**

Data integrity can be defined as the validity of data and their relationships. For electronic records collected and processed as part of a clinical trial to be trustworthy and reliable, the links between raw data, metadata, and results must not be compromised or broken. Without data integrity, it is not possible to regenerate a previous result of a clinical trial reliably.

Obviously, maintaining data integrity is an important aspect not only for clinical trials and eClinical Platforms. This needs to be addressed throughout the product lifecycle spreading across GMP, GLP, GCP and other GxP areas.

In considering all of these aspects, it becomes obvious that data integrity cannot be ensured by the validation of the individual systems and their point-to-point interfaces alone. A more holistic approach toward validation, including relevant processes, data and quality management is necessary because those systems are acting together across corporate borders and controlled by different quality systems. Similar to validating individual systems following a risk-based approach, the risks of using the eClinical Platform must be identified, assessed and adequately addressed.

In addition to the system and study life cycles, this holistic validation approach needs to support the complete data life cycle from the first generation of the data until the end of the retention periods and should include the relevant metadata. To limit the scope of this excerpt, only the validation aspects of the systems and platforms are investigated. Other techniques and controls need to be in place to assure data integrity along the complete data life cycle.
3 Generic eClinical Platforms vs. Trial-Specific eClinical Platforms

As it would be inefficient to build a full eClinical Platform for every trial, establishing a generic eClinical Platform based on the individual GCP systems is required.

A generic eClinical Platform consists of all potentially required systems for the conduct of a clinical trial (Figure 3.1). These are typically connected via numerous interfaces. Basic functionality and configuration that is required for the majority of clinical trials is included and validated following a risk-based approach.

This generic eClinical Platform also includes all SaaS offerings and systems from strategic partners like CROs that are frequently used for the conduct of clinical trials. The necessary transfer of data between the clinical trial site, CRO and sponsor adds significantly to the complexity of the platform.

This generic eClinical Platform provides the validated baseline for any trial-specific platform and additional validation activities. This validated baseline enables organizations to establish a "trial-specific" eClinical Platform in a timely manner as only aspects that differ from the baseline need to be validated for the setup and configuration of the trial.

Depending on the type and complexity of the clinical trial, this trial-specific eClinical Platform may only contain a subset of the systems offered by the generic eClinical Platform and includes trial-specific setups and configurations of these systems. Furthermore trial-specific requirements may require the development, set-up and/or configuration of trial-specific interfaces within the organization and/or between organizations.

4 The Foundation - Validation of the Individual Systems

The validation of the individual systems forms the foundation of all further quality management activities.

As illustrated in Figure 4.1, the platform life cycle is based on the general requirements that would support a generic clinical trial. Therefore, in order to assess the validation for systems used in the context of a clinical trial an assessment of the general underlying platform life cycle as well as the trial-specific life cycle is necessary.

The trial life cycle is based on the trial-specific requirements as determined by the team supporting and executing an individual clinical trial project.

Depending on the type and function of the system, the validation effort may be greater for the platform life cycle than the trial life cycle aspects (e.g., safety systems typically require only very limited setup and configuration to address trial-specific needs as the processing of Serious Adverse Events (SAEs) is quite uniform and regulated in fine detail). In contrast, the trial-specific setup of an EDC system, including the necessary electronic Case Report Forms (eCRFs), often requires significantly more effort while only basic functionality can be validated as part of the platform life cycle.

However, without the integration with other systems, these individual systems are just isolated building blocks that would not appropriately support the various processes necessary for a clinical trial. Only through integration with other systems can they truly form an eClinical Platform. Obviously any automated transfer of data via interfaces to systems that potentially support a different part of the business process can add risks for the integrity of data as well.
5 Interfaces (Technical Aspects)

Interfaces may be between internal systems or reach across multiple organizations. The setup often includes systems from the sponsor, CRO(s), various suppliers including EDC providers, laboratories, electronic Patient Reported Outcomes (ePRO) providers, logistics and others. Additionally, systems at the investigator site like EHR systems may be included in the eClinical solution.

While integrated systems of the same organization are usually very well controlled, the setup, operation and maintenance of interfaces between different organizations are more challenging. This requires well-established communications and sound contractual agreements to address potential differences in the validation approach and agreement on standards to be used. These arrangements are typically more mature between trusted partners that are considered to be reliable, trustworthy and have been utilized and audited several times. Typically, these partners have the status of a preferred supplier/vendor and there is a well-established Service Level Agreement (SLA) in place.

6 Interfaces (Organizational Aspects)

Ensuring the integrity of data collected and managed by a computerized system is essential to support the evaluation of the investigational product and ultimately protect patient safety. As stated in ICH E6 Guideline for Good Clinical Practice, “the ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor,” therefore, the sponsor has to establish adequate quality oversight.

The current trend of pharmaceutical companies to outsource significant parts of their clinical trial activities and IT systems often leads to a complex eClinical Platform involving several partners, one or more CROs and several IT providers.

Generally, open and honest communication between all involved partners are essential for the success of an eClinical Platform and subsequently the success of the trials conducted. Therefore, not only are contracted items crucial for data integrity throughout the entire trial life cycle, but also the contact between the responsible project’s personnel involved in the trial. Regular meetings (e.g., weekly, biweekly, etc.) during the trial life-time are essential. Furthermore, the participation of all relevant parties, including business, IT and quality is crucial as systems and trial setup are likely to change over time. A good team, managed by project managers from the sponsor and the supplier(s), is a key factor for the success of the trial and maintaining data integrity.

Another important aspect is that the supplier(s) fully understand the regulations that the sponsor must comply with, and that they have a vital part in ensuring that compliance is maintained. This includes supporting audits and inspections by the supplier and/or regulators, but also the timely reporting of incidents to the sponsor. The criteria for reporting of incidents may be documented within a contract.

Note: The protection of personal data and patient confidentiality as well as the blinding/unblinding of data pose additional challenges.

However, it also must be understood that the intellectual property of the involved partners must be protected, as some partners may be competitors in the same market. For example, a sponsor may work with several CROs or EDC providers. This should be considered throughout all communication channels when multiple parties are involved.

7 Validation in Different Organizations

Every interface can potentially endanger the data integrity of a trial. Consequently, all interfaces and systems should be assessed and validated following mutually acceptable standards. This is often very difficult to verify, achieve, or establish if the eClinical Platform involves systems validated by different organizations following their own internal standards and procedures.

Terminology is often used inconsistently across various parties and thereby produces additional challenges in communication. A mapping of the individual validation deliverables and terminology to the GAMP® 5 Guide can establish transparency and identify gaps. This can be done as part of regular audits or as part of on-going communications between the involved organizations.

Sponsors may consider establishing a “Quality Committee” with representatives from all strategic/preferred partners to define requirements and develop a common approach. This committee may also ensure that all partners are aware of the most recent changes in relevant regulations. It is noteworthy that recent guidance released by the U.S. Food and Drug Administration (FDA) explicitly states that FDA does not intend to assess the compliance of EHRs with 21 CFR Part 11 [6].

8 Data Flow and End to End Validation

Aristotle is attributed as saying: “The whole is more than the sum of its parts.”

In this context, even if every involved system for every involved partner has been validated to standards and processes, including clearly defined risk-based approaches, this may still not be enough to ensure the mutually agreed integrity of data.

The remaining risk results from the fact that the data are not just being exchanged between two systems or two parties. Some of the data flows through multiple systems at multiple partners, as illustrated in Figure 8.1.

Figure 8.1: Data Flows in eClinical Platforms
The individual teams responsible for a system are often aware of the immediate partners or systems with which they exchange data. However, most of the time, they are unaware of any further handovers or data transfers. Therefore a change in System A, or the processes applicable to System A, may not have an effect on the directly interfaced System B. But it may very well be having an effect on System C that is interfaced with System B.

Obviously this could be avoided if every system would “read” the required data directly from the source. However, this might not be possible for either procedural and/or legal reasons.

**An Example:**
A trial start-up tool provides site data (i.e., name, contact details, etc.) to the CTMS. At this point in time, these sites have not been “initiated,” as they are imported into the CTMS as “ready for initiation.” Once the initiation is completed, the data are transferred to the EDC system and the sending of login details is triggered.

A change in the way the data are collected in the trial start-up tool (e.g., fax numbers are no longer captured) may not have direct consequences in the CTMS (as the users use other means of communication such as e-mail, etc.); however, it could trigger problems in the EDC system (as it sends the user name via e-mail but the initial password via fax).

Data that are often transferred in such a way includes:
- Investigator data
  - Often processed in CTMS, EDC, IVRS/IWRS and financial systems
- Site data
  - Often processed in CTMS, EDC, IVRS/IWRS and trial start-up tools
- Safety data
  - Often processed in CTMS, EDC, and safety systems

As a consequence, data integrity is at risk. However, the integrity of the data could be established by an end-to-end verification of the eClinical Platform.

This could be achieved by setting-up a trial in the test environment of the full eClinical Platform. In this setup, all processes changes for the systems, or for the trial, could be tested prior to “release to production” in order to mitigate risk to data integrity. However, this is a rather costly approach.

Alternatively, if data flow could be analyzed along the clinical processes, the risks associated to these data flows could be determined. This would require a much more detailed analysis of the processes, data and records than it is typically done today. Furthermore it would require a Review Board that would be able to carry out extensive impact and risk assessments of each change request.

It must be understood that these activities are not limited to automated data transfers. Quite often data are transferred at specific intervals or at specific milestones of the project by “manual” handovers. An example would be the handover of the locked database content from data management, at a CRO, to the sponsor or other party for further analysis. This is often done via a manual upload to a secure File Transfer Protocol (FTP) site.

**9 Summary**
With the on-going trend for outsourcing clinical trial activities, the risks to data integrity become higher and more visible.

Tightly integrated eClinical Platforms spanning across multiple organizations have been established over time and should be considered a standard practice. The tightly integrated flow of data between multiple systems requires additional controls to ensure data integrity during the data creation and collection stage of the overall clinical data lifecycle.

Foremost the importance of cross-organizational communication cannot be underestimated. It has become apparent that significantly more effort is required by the sponsor than to just conduct regular audits. Due diligence and regular audits of the supplier(s) are no substitute to active partnership and cooperation.

Contractual agreements are critical to ensure a common understanding of the expectation for each party involved. They need to go significantly beyond the mere financial details and a high level scope of the work to be done. Quality standards and communication aspects should be included at this stage as well.

In addition, a risk-based approach to validation must not only be applied to individual systems, but also must be taken upward to the next level. A holistic risk Assessment of the eClinical Platform, including data flows across integrated systems, must be performed with additional controls added as necessary. This can include processing of a trial in a test setup of the platform or end-to-end tests across the eClinical Platform for critical data flows.

The most suitable approach must be determined for each eClinical Platform on an individual basis, as they vary greatly in complexity. As with most systems, the greater the complexity the greater the risks, and the more necessary additional controls are to implement.

While this article specifically addresses some of the technical and organizational aspects data integrity, the impact of human error or fraud to the integrity of data is not covered. These aspects require additional thought and should be discussed separately.
Advertising Opportunities in ISPE CaSA 2015 Electronic Newsletter

The ISPE CaSA Chapter produces six e-newsletters per year. ISPE CaSA sends out the newsletters via e-mail and via Web link to all of our Chapter Members throughout the Southeastern U.S., which reach top-notch pharmaceutical, biotechnology, and bio-science professionals and managers. These newsletters are also posted on our Web site so your ad can be accessed by interested visitors to our site.

The cost for a full color business-card-sized ad is $750 per year. There is also the ability of positioning your ad on the front page of the newsletter for an additional $750 per year for six issues. Space limits the number of front page to only four, and is offered to the first four paid advertisers on a first-come, first-served basis.

Also, if you would you like to have your targeted customers go directly to your website by simply clicking on your ad; a hot-link can be added to your submitted ad file for an additional $500.00 for the entire year.

You may choose one of the special offers below: 
• $1,500 Full-color ad for six issues on the front page of each newsletter ($250/issue)
• $1,500 Full-color double-sized ad for six issues ($250/issue)
• $750 Full-color ad for six issues ($125/issue)
• $200 Full-color ad in 1 newsletter of your choice
• $500 Adding a hot link for directing customers to your website by a simple click

We hope you will take advantage of these opportunities and advertise in the 2015 ISPE CaSA e-newsletter.

To reserve a placement of your ad for 2015 please contact the ISPE-CaSA Headquarters at 919-573-5442 or via e-mail at info@ispecasa.org. Deadline for 2015 advertisers to be in the February 2015 issue is January 23.

You will be notified via e-mail or telephone when your advertisement has been accepted by the ISPE-CASA Newsletter Committee and asked to submit your advertisement digitally. Full-color business card-sized ads (3.5” x 2”) may contain your logo or other artwork. Artwork should be sent directly to newsletter@ispecasa.org.

We ask that your text be no smaller than 12 pt so that the text is easily readable in the electronic format. PDF, JPEG, or TIF formats, are easiest for us to work with. Space is limited, sign up today!
Now you can reach www.ispe-casa.org audience by advertising on our website. A limited number of advertising spots are now available so don’t delay. Contact the ISPE Carolina-South Atlantic Chapter to reserve your space.
(Please note: ISPE-International-forbids website ads on our chapter’s home page, so they are on subsequent web pages.)

To learn more about this opportunity, contact Penney De Pas, Chapter Manager, at 919-573-5442 or pdepas@ispecasa.org. If you are interested in signing up for the program, please complete the form and return to pdepas@ispecasa.org or fax 919-787-4916. Advertisements are sold on a first-come first-served basis.

**SPECS OF ADVERTISEMENT:**

Top Placement Ad 120 pixels wide by 240 pixels high; File formats accepted: .GIF, .JPG, .SWF
Bottom Placement Ad 240 pixels wide by 400 pixels high; File formats accepted: .GIF, .JPG

<table>
<thead>
<tr>
<th>Advertisement Type</th>
<th>12 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>240 x 400 Vertical Rectangle</td>
<td>$500</td>
<td>$300</td>
</tr>
<tr>
<td>120 x 240 Vertical Banner animated</td>
<td>$400</td>
<td>$250</td>
</tr>
<tr>
<td>120 x 240 Vertical Banner - non animated</td>
<td>$300</td>
<td>$200</td>
</tr>
</tbody>
</table>

- □ 240 x 400 Vertical Rectangle ad 6 Months, $300
- □ 240 x 400 Vertical Rectangle ad 12 Months, $500
- □ 120 x 240 Vertical Banner animated ad 6 Months, $250
- □ 120 x 240 Vertical Banner animated ad 12 Months, $400
- □ 120 x 240 Vertical Banner - non animated 6 Months, $200
- □ 120 x 240 Vertical Banner - non animated 12 Months, $300

Name: ___________________________________________ Member #: ____________________
Company: ___________________________________________
Title: _________________________________________
Address: ___________________________________________ State: _______ Zip: _______
Tel: __________________________ Fax: __________________
Email: __________________________

**PAYMENT TYPE:** □ Visa □ MasterCard □ AMEX
Or □ Check (Payable to: ISPE-CASA)
Card #: ______________________ Expiration Date: __________
Cardholder Name (as it appears on card): __________________________
Cardholder Signature: __________________________

1500 Sunday Drive, Suite 102, Raleigh, NC 27607-5151 * phone (919) 573-5442 * fax (919) 787-4916 * email info@ispecasa.org
ISPE CaSA Chapter E-Newsletter Ads

Newsletter Ads Work for Your Business!

Our Chapter produces six e-newsletters per year, and we depend on the support of our advertisers. We send out the newsletters via e-mail and via web link to all of our Chapter Members throughout the Southeastern U.S. That means you get targeted access to top-notch pharma, biotech, and bio-science professionals and managers. These newsletters are also posted on our website so your ad can be accessed by interested visitors to our site.

Best of all, the cost is only $650 for your full color, business-card-sized ad for six insertions. That’s only $650 for targeted advertising in full color for an entire year!

Ask About HOT LINKS!!

Would you like to have targeted customers simply click on your ad and get right to your website?

A hot-link can be added to your ad, connecting readers directly to your company website for an additional $500.00 for a whole year.

If you are interested in advertising with the ISPE CaSA e-newsletter, please contact our Chapter headquarters at:

ISPE-CaSA
1500 Sunday Drive, Suite 102
Raleigh, NC 27607
919-573-5442
info@ispeCaSA.org

You will be notified via e-mail or telephone when your advertisement has been accepted by the ISPE CaSA Communications Committee and asked to submit your advertisement digitally.

Full-color business card-sized ads (3.5” x 2”) may contain your logo or other artwork. Artwork should be sent directly to info@ispeCaSA.org.

We ask that your text be no smaller than 12 pt so that the text is easily readable in the electronic format. PDF, JPEG or TIF formats are easiest for us to work with. Space is limited, sign up today!

EDITORIAL POLICY

Articles should be written for technical professionals in the pharmaceutical, biotechnology, and medical device industries. The author is responsible for the accuracy and correctness of all statements contained in the manuscript (ISPE Carolina-South Atlantic Chapter assumes no liability.) Manuscripts should be forwarded to a Member of the Communications Committee at rich.stanfield@cagents.com for review 30 days prior to publication. A brief three to four sentence synopsis of the article, as well as a brief biographical statement about the author that includes educational background, title and job affiliation, job responsibilities and major areas of accomplishment must accompany the article.

Got News?

Send it to: rich.stanfield@cagents.com

Entries should be brief and be of general interest to the readership.

Entries must include a name and telephone number for verification purposes.

We reserve the right to edit and select entries.

A word to the ISPE CaSA Newsletter advertisers:

Thank you all for your continued support. Without it we could not have the wonderful support staff to get our ISPE CaSA Members the news in such a timely and professional fashion. If you have updates to your advertisements or find any other error, please contact us so that we can serve you better.