APRIL 2017

Clinical Researcher™

The Authority in Ethical, Responsible Clinical Research

Technology for Trials:

Are You Falling Behind, Keeping Up, or Getting Ahead?

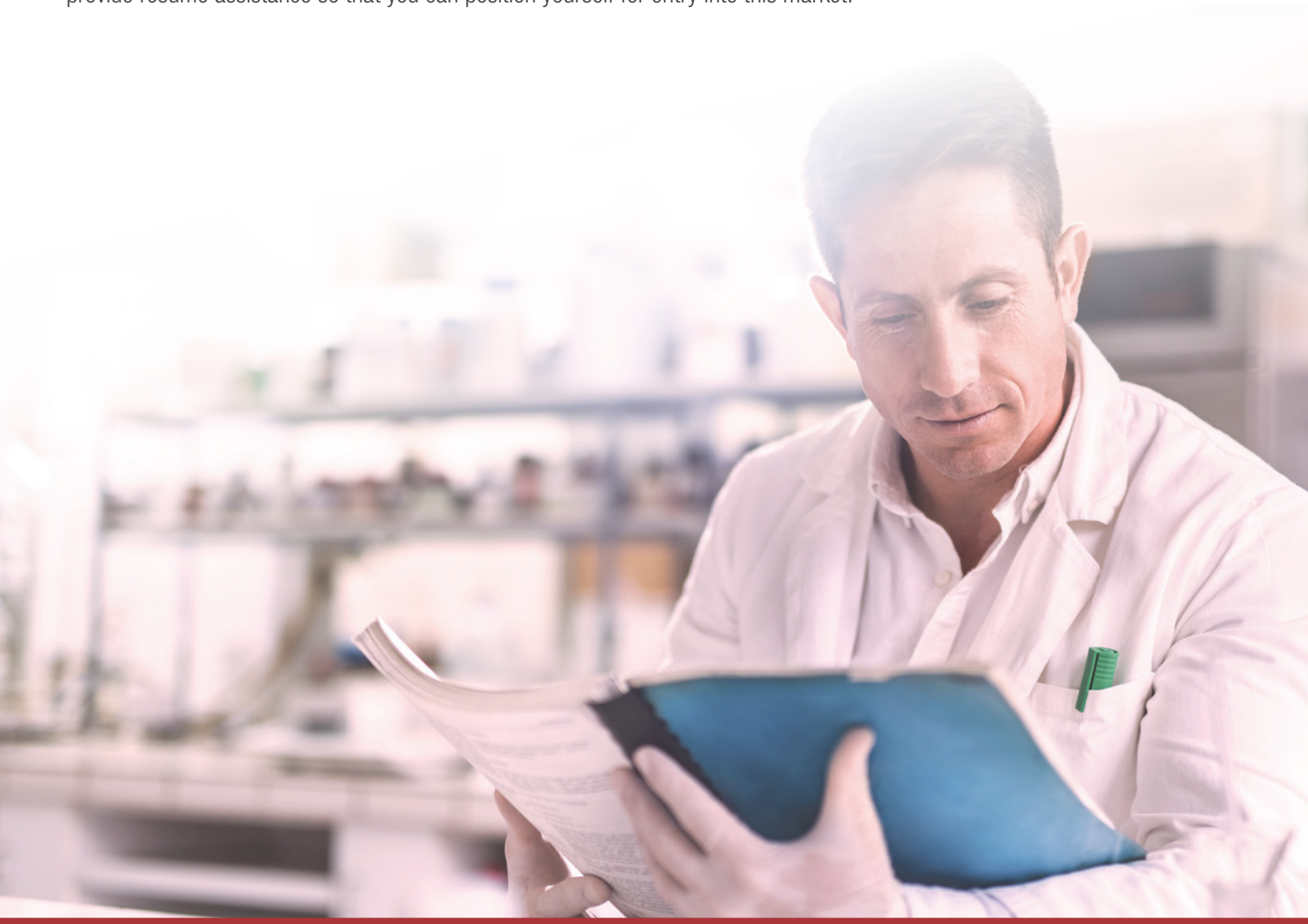
INCLUDING the Latest in Workforce Innovation

Association of Clinical Research Professionals (ACRP)
www.acrpnet.org

BARNETT INTERNATIONAL
Leaders in Clinical Research Training

10-Week CRA & CRC Beginner Program

The online 10-Week CRA & CRC Beginner Program provides a comprehensive introduction to clinical research and the job functions of the Clinical Research Associate (CRA) and Clinical Research Coordinator (CRC) for drug, biologic, and device trials. This program is geared toward individuals seeking a new career or career change into clinical research, but haven't decided which job track to pursue. Case studies and industry best practices are presented to emphasize how the learning objectives apply directly to the responsibilities of the CRA and CRC. Upon completion, Barnett will provide resume assistance so that you can position yourself for entry into this market.



At PRA, our CRAs don't just become experts at driving the data that brings safe drugs to market, **they become experts at driving their career.**

"Being a CRA taught me all the skills I needed to shift behind the scenes. All the data and information that was always so fascinating to me is now what I get to use to make our studies better."

Few PRA employees know this better than Lee Lubertazzi. Starting her career as an in-house CRA, and then going through PRA's BRIDGE program to become a CRA, Lee has always had a passion for data. "As a person who appreciates precision, I've always found data and chemistry fascinating. Exact science – that's what I'm really great at."

Realizing that she had a job that she loved and a growing family she adored, Lee wanted to find the perfect balance. She wanted to keep making a difference, keep getting safe drugs to market, and keep ensuring all the data our CRAs were diligently gathering was being used effectively. As PRA shifted to an adaptive monitoring model, Lee knew that her degrees in math and chemistry, her passion for precise science, and the technology and analysis skills she had mastered as a CRA would make her a perfect fit for a new role within the adaptive monitoring model – a clinical monitoring associate (CMA).

While it wasn't a new concept, the idea of using site-experienced, highly skilled CMAs was new to the industry. Working remotely, the CMA would monitor sites, check on vendors, facilitate site communication, and analyze valuable data to enable more efficient and effective studies. Even though she knew she'd be taking a risk, Lee decided to take the leap to become PRA's very first CMA.

And, if one person knows the role of a CMA at PRA, it's Lee. That's because she's defining it.

Using a new approach to examine the data she was already using as a CRA and calling on the remote site communication skills she acquired as an in-house CRA, Lee has not only found success in her role as a CMA but has helped PRA grow the role to 20 CMAs throughout the company. Because of her translatable CRA skills and the dedicated support from her functional manager, Lee had a fluid transition to her new data-focused responsibilities. She's even helped to develop the tools, processes, and procedures for the group.

She's influencing change not only at PRA but our entire industry.

Through her move from CRA to CMA, Lee has never lost sight of what keeps her passionate. She knows how important it is to ask the right questions and gather good data for drug development. If drugs are approved that shouldn't be, someone could get hurt. If drugs aren't approved that should be, we miss out on the chance to make a positive impact on countless lives. For some people, the implications of good data are life altering. Lee's attention to detail, site communication, and data analysis skills made her the perfect candidate to bring the CMA role to life and help it grow in our company. Lee's own growth at PRA has made her a pioneer in this industry.

Learn more about driving your own career in clinical research and available opportunities at PRA by visiting our talent acquisition team at booth #205.

PRAHEALTHSCIENCES

Clinical Researcher™
The Authority in Ethical, Responsible Clinical Research

CONTENTS

April 2017 • Volume 31, Issue 2 • ISSN 2334-1882

Feature PEER REVIEWED

Workforce Innovation

Clinical Researcher is your platform. Interested in writing a peer-reviewed article or guest column? You'll find our submissions guidelines at acrpnet.org/submit

Cover image: iStock.com/monsitj

ACRP
FOR LEARNING FOR LISTENING FOR LIFE

Clinical Researcher ISSN 2334-1882 (Print) and ISSN 2334-1890 (Online) is published bimonthly. It is provided to ACRP members by the Association of Clinical Research Professionals (ACRP). The views, research methods, and conclusions expressed in material published in *Clinical Researcher* are those of the individual author(s) and not necessarily those of ACRP.

Postmaster: Send address changes to Clinical Researcher
99 Canal Center Plaza, Suite 200, Alexandria, VA 22314

+1.703.254.8102 (fax)
+1.703.254.8100 (phone)

www.acrpnet.org

DESIGN
TGD Communications
tgdcom.com

[DOI: 10.14524/CR-17-4014]

MANAGING EDITOR'S MESSAGE
Gary W. Cramer

Indiana Jones and the Avoiders of the New Tech

"Technology... Why did it have to be technology?"

Gary W. Cramer (gcramer@acrpnet.org) is managing editor for ACRP.

Just imagine me saying that in my best Indiana Jones voice and it might be kind of funny, because new technology is to me what snakes are to that fictional archaeologist. This near-phobia on my part goes back at least as far as my first day taking a college-level journalism course in 1985, when the faculty leader plopped all of us students down in front of manual typewriters, insisting that the only way to learn how to write on deadline was to do it without the "luxury" of word processors—and I was kind of relieved.

These days, occasional old school reluctance to dive into using them aside, I'm glad to say that I have the best in modern word processing and in-office publication tools at my disposal—no whiteout needed. I may be stuck at PlayStation 2 levels of entertainment at home, but at work I've got what I need to get the job done. This brings us to the theme of this issue, focusing yet again on tech-related trends and insights for the clinical research enterprise, since there's just no escaping the impacts of new and improved technology on the conduct of clinical trials.

In the pages ahead, you'll learn about data management tools and tactics, regulatory expectations, best practices in study coordination, and tips for just getting through the work day that all tie back to where the wonderful world of technology has brought us to date. Many thanks to our article and column authors, and to the article-soliciting powers of ACRP Editorial Advisory Board member Shirley Trainor-Thomas, for making this issue possible.

We want to hear from you. Is technology making your role in clinical research better? More challenging? Or are you still waiting for the decision makers where you are to adopt the tech you think your site needs? Please feel free to send your letters to the editor on this or any other topics to editor@acrpnet.org, and we'll run the best ones we receive in future issues.

ACRP
FOR LEARNING FOR LISTENING FOR LIFE

EXECUTIVE DIRECTOR'S MESSAGE
Jim Kremidas

[DOI: 10.14524/CR-17-4015]

Helping You Keep Pace with the Speed of Change

These are exhilarating times in our industry. Whether it's improvements in remote monitoring practices, advances in informed consent and patient-centricity, or the professionalization of the clinical trial workforce, change is coming at a dizzying pace.

Jim Kremidas (jkremidas@acrpnet.org) is the Executive Director of ACRP.

ACRP is dedicated to helping you thrive today and tomorrow. We'll be with you every step of the way with new training, new resources, and new ways of benchmarking performance based on skill and not just tenure.

We'll be announcing several initiatives at our 2017 Meeting & Expo this month in Seattle. Each is designed as part of ACRP's overall goal to better define and advance the important evolving roles played by clinical research associates (CRAs), clinical research coordinators (CRCs), principal investigators, project managers, and other stakeholders in the clinical research enterprise.

Many of you have already participated in the development of these initiatives. I'm looking forward to discussing the new programs and strategies with more of you at the conference and other venues later this spring and summer. We'll also spread the word via our website, Facebook page, *CRbeat,* and the June issue of *Clinical Researcher.* We encourage feedback from everyone.

Partners in Progress

Meanwhile, we continue to add members to our multistakeholder Workforce Development Task Force, including broad representation from leading industry and academic organizations across the global clinical research enterprise. As this issue of *Clinical Researcher* went to press, we've been joined by a number of pioneers, including:

- Celgene Corporation
- Advanced Clinical
- ACRO (Association of Clinical Research Organizations)
- Medtronic
- Cancer Research UK
- Merck & Co.
- AstraZeneca

I'm also proud of ACRP's work with the Clinical Trials Transformation Initiative (CTTI). Together, CTTI, ACRP, and other companies and organizations are helping to raise the bar for improving research performance. However, we've just gotten started.

CTTI Executive Director Pamela Tenaerts, MD, MBA, put it best in CTTI's 2016 Annual Report: "While significant advancements have been made, many opportunities remain to improve clinical research."

ACRP will be working closely with CTTI and other important industry voices this year to collect and share information on increased adoption and implementation of recommendations backed by real-world examples. For example, under the new e-consent model, clinical trial practitioners will follow literacy best practices, which includes using multimedia formats such as video to address a variety of learning types and improve overall patient comprehension for every current and potential trial participant.

There's more good news to share: Thanks to a new partnership with Barnett Educational Services, ACRP members now have access to the full catalog of webcast and in-person Barnett training programs at an *exclusive 10% discount.*

Keep Listening, Keep Learning

Finally, I hope you've had a chance to listen to the recent release of our first ACRP Clinical Trial Insights podcast, or if not, you can find it on the ACRP website under News & Events.

The first podcast episode features Ken Getz, associate professor and director of sponsored research with the Tufts Center for the Study of Drug Development; David Vulcano, LCSW, MBA, CIP, RAC, with HCA (Hospital Corporation of America); and myself as we discuss how to navigate the new landscape in the clinical trial industry.

In future podcasts, we'll look at the promise of the paperless office and will share insights and feedback from many of you who attended the conference. If you have an idea for a topic or speaker you'd like us to feature, please let us know. Feel free to stop by our ACRP booth in the Expo Hall during the conference to let us know how we can do a better job supporting you today and tomorrow.

I'm looking forward to seeing you in Seattle.

Stop by our ACRP booth in the Expo Hall during the conference to let us know how we can do a better job supporting you today and tomorrow.

CHAIR'S MESSAGE

Jeff Kingsley, DO, MBA, CPI, FACRP

[DOI: 10.14524/CR-17-4012]

It's About the People, People!

ACRP is taking the lead in tackling some of the thorniest and most neglected issues affecting our industry today. By this, I mean people issues. For any organization to run effectively in terms of fulfilling its mission, it must have an appropriate strategy, a structure capable of efficiently achieving that strategy, and people capable of executing exceptionally well.

"Talent is the No. 1 priority for a CEO. You think it's about vision and strategy, but you have to get the right people first."
—Andrea Jung

Jeff Kingsley, DO, MBA, CPI, FACRP, (jkingsley@iacthealth.com) is chief executive officer of IACT Health in Columbus, Ga., and Chair of the 2017 Association Board of Trustees for ACRP.

The strategy is unique to each individual organization. The structures within each organization include its policies and procedures, its processes, technology, key performance indicators, dashboards, reporting hierarchy, and all of the other facets necessary to run an organization.

A great deal of work has been done by ACRP and others in the clinical research enterprise on implementing and improving these structures with the goal of having organizations involved in clinical trial conduct on all sides of the equation work together better—sponsors, sites, contract research organizations (CROs), technology vendors, regulators, patient advocacy groups…you name it. However, a phenomenal strategy and exceptional structures will still produce a poor result without a significant effort in ensuring that the right people are on the research team, that those people have been trained appropriately, and that they have all the necessary resources to win.

Professionalizing the Profession

Your Association has been active in its work to help formally "professionalize" the clinical trial industry. Earlier this year, for example, ACRP unveiled a major initiative to promote and validate competence in clinical research (see https://www.acrpnet.org/professional-development/competency-domains-clinical-research-professionals/).

ACRP's industry-leading certification programs have been harmonized with the Core Competency Framework developed by the Joint Task Force (JTF) for Clinical Trial Competency, whose contributors and collaborators include leading organizations representing clinical research sponsors, CROs, sites, and academia. By aligning its certification programs through exam content with the JTF competencies, ACRP promotes and validates competence in the clinical research workforce. Much of the work being done now aims to define the core competencies required of clinical trial monitors/clinical research associates within the eight core competence domains for clinical research professionals, as defined by the JTF (see https://www.acrpnet.org/monitoring-competencies/), and the industry is already taking notice, as you can read more about in the Workforce Innovation section of this issue.

These and other workforce initiatives will be discussed at the ACRP 2017 Meeting & Expo this April 28–May 2 in Seattle, Wash., the sessions of which are also organized by tracks aligned with the core competencies concept (see http://conference.acrpnet.org/). I urge you to come to the conference and join the conversation. Among many other features, this year's event offers experts from across the field participating in a unique Signature Series of sessions on how process, technology, and workforce innovation are shaping the current and future state of clinical research.

Hungry for More?

Peter Drucker, the famous business management guru, said "culture eats strategy for breakfast"; and with this in mind, we would do well to remember that culture is the people side of business. I know that in my company, the people side of business is always the most challenging. I am thrilled that ACRP is taking the lead in workforce development, and I'm proud to be able to participate in the valuable work that our organization is undertaking.

HOME STUDY TEST

Earn 3.0 Continuing Education Credits

This test expires on April 30, 2018

(original release date: 4/1/2017)

In this issue of *Clinical Researcher*, the three articles that follow this page have been selected as the basis for a Home Study test that contains 30 questions. For your convenience, the articles and questions are provided in print as well as online (members only) in the form of a PDF. This activity is anticipated to take three hours.

Answers must be submitted using the electronic answer form online (members only, $60). Those who answer 80% of the questions correctly will receive an electronic statement of credit by e-mail within 24 hours. Those who do not pass can retake the test for no additional fee.

ACRP DISCLOSURE STATEMENT

As an organization accredited by the Accreditation Council for Continuing Medical Education (ACCME®), the Association of Clinical Research Professionals (ACRP) requires everyone who is in a position to control the planning of content of an education activity to disclose all relevant financial relationships with any commercial interest. Financial relationships in any amount, occurring within the past 12 months of the activity, including financial relationships of a spouse or life partner, that could create a conflict of interest are requested for disclosure.

The intent of this policy is not to prevent individuals with relevant financial relationships from participating; it is intended that such relationships be identified openly so that the audience may form their own judgments about the presentation and the presence of commercial bias with full disclosure of the facts. It remains for the audience to determine whether an individual's outside interests may reflect a possible bias in either the exposition or the conclusions presented.

80% The pass rate for the Home Study Test is now 80% to be in alignment with ACRP professional development standards.

CONTINUING EDUCATION INFORMATION

The Association of Clinical Research Professionals (ACRP) is an approved provider of medical, nursing, and clinical research continuing education credits.

Contact Hours

The Association of Clinical Research Professionals (ACRP) provides 3.0 contact hours for the completion of this educational activity. These contact hours can be used to meet the certifications maintenance requirement. (ACRP-2017-HMS-004)

Continuing Nursing Education

The California Board of Registered Nursing (Provider Number 11147) approves the Association of Clinical Research Professionals (ACRP) as a provider of continuing nursing education. This activity provides 3.0 nursing education credits. (Program Number 11147-2017-HMS-004)

Continuing Medical Education

The Association of Clinical Research Professionals (ACRP) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The Association of Clinical Research Professionals designates this enduring material for a maximum of 3.0 AMA PRA Category 1 Credits™. Each physician should claim only the credit commensurate with the extent of their participation in the activity.

OPINION:

DATA – The Foundation of Clinical Trials

PEER REVIEWED | Richard Young

[DOI: 10.14524/CR-17-0003]

A changing world brings data to the forefront, but how do we manage it all to make the biggest impact?

The life sciences industry has been fundamentally altered in recent years. Diseases that were once considered life threatening and terminal are now being managed as chronic conditions. Previous chronic illnesses are treatable and curable, while other diseases have been reduced to irritations or consigned to the history books.

Clearly, there is much to celebrate, but there is still much to do. Advanced solutions are needed to treat such conditions as multiple cancers, heart disease, obesity, Alzheimer's, and Parkinson's, to name a few. The speed of innovation and the acceleration of new solutions to market will be increasingly important.

Within pharmaceutical companies, the quest for understanding has accelerated, leading to the establishment of a knowledge-based economy with data as the currency. The more we know, the more we can develop these advanced solutions to not only meet, but get ahead of expectations.

Scientific breakthroughs will continue the more we understand the human body—not just the biochemical pathways, systems, and organs, but also the inter- and intrapersonal behaviors that form our very makeup. This process will accumulate vast quantities of data, especially in clinical trials.

As the volume of clinical data rises, the ability to turn those data into quick decisions is limited by today's technology approaches, including electronic data capture (EDC) systems. Consequently, sponsors and sites are not equipped to support new and innovative trial designs, such as adaptive clinical trials.

Making complete and accurate data available will enable life sciences researchers to finally run the trials they want, not the trials today's EDC systems allow. If clinical researchers can have their data in real time, the life sciences industry can better address the problems that are leading to distress, illness, and even death. It is the accumulation and conversion of these data into actionable insights that will drive the era of personalized or precision medicine.

Major Shifts Impacting the Industry

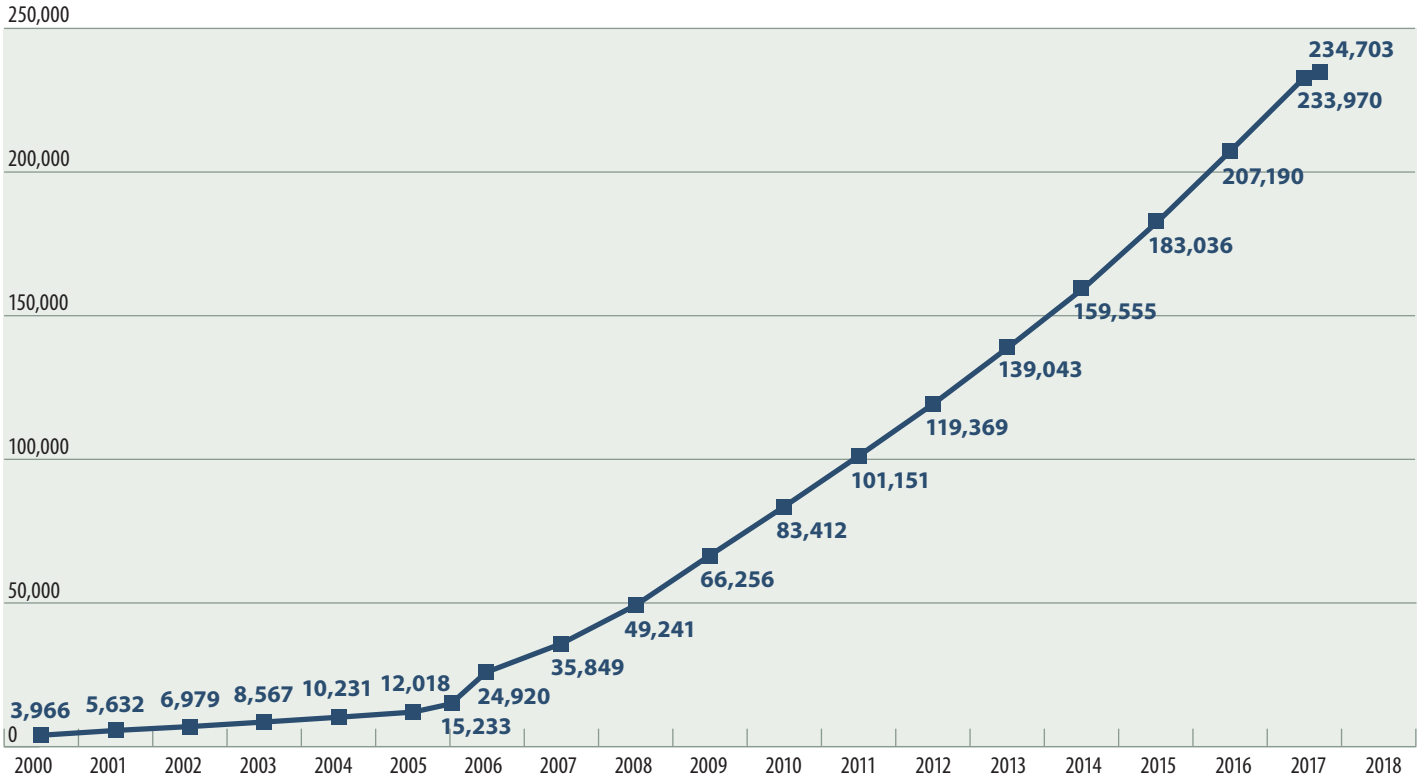
THE RISE OF PERSONALIZED MEDICINE

The industry has long discussed the end of the blockbuster era, which raises the impending need for life sciences companies to find avenues for bringing products to market other than through a narrow focus on potential mega-selling therapies.

LEARNING OBJECTIVE
After reading this article, participants will be able to discuss the importance of turning raw data into actionable insights and decisions for patients in the medical development industry.

DISCLOSURES
Richard Young:
Nothing to disclose

FIGURE 1: Number of Studies Registered with FDA Over Time (as of January 17, 2017)



Source: U.S. Food and Drug Administration (FDA)

In January 2017, ClinicalTrials.gov showed that since 2014, the number of registered clinical studies has increased by almost 50% (see Figure 1). Likewise, new records for U.S. Food and Drug Administration product approvals were consecutively set in 2014 and 2015.

It is easy to conclude that more trials, reaching more patients, and generating more data are resulting in more products to market, but in 2016 that trend was reversed (see Figure 2). This speaks to a rapidly changing environment, and highlights the need for yet more innovation.

Further exacerbating the challenge for manufacturers are looming patent cliffs for many of their top products; in 2016, several high-profile, brand name products were slated to lose patent protection. Patent expirations for highly prescribed medicines will continue to influence healthcare spending as lower cost generics are allowed to compete in the larger marketplace and drive down costs. Although it depends on the type of treatment, the average price of a generic can be as much as 85% lower than its patented brand name counterpart.[1] In fact, between 2009 and 2014, more than $120 billion in pharmaceutical sales was lost to patent expirations.[2]

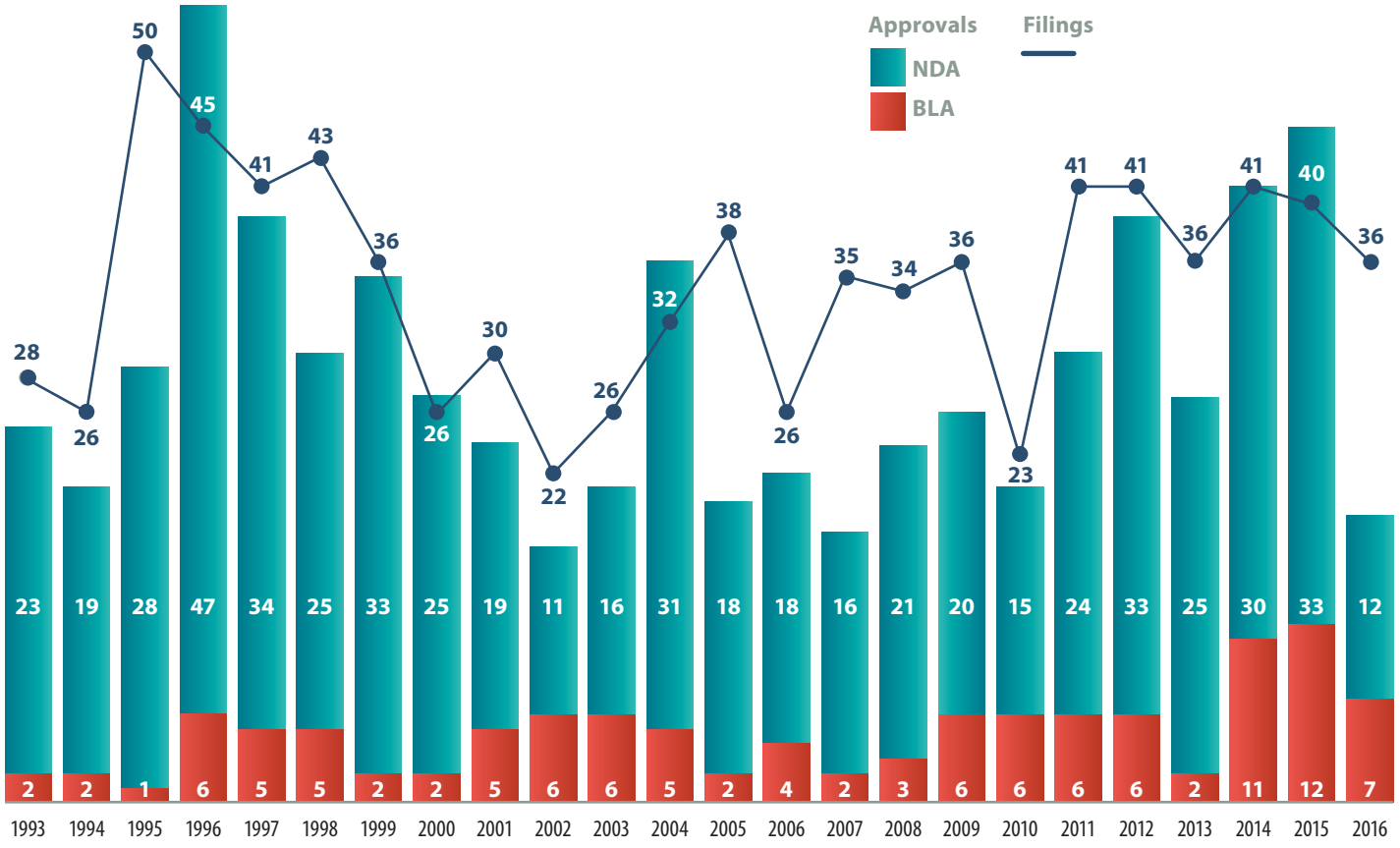
AN INCREASED FOCUS ON PATIENT OUTCOMES

Another major change is linked to consumption models and patients. With every new scientific development, there is renewed expectation of long-term benefit. Armed with heightened anticipation, patients don't buy drugs anymore, they buy outcomes. This means manufacturers will see their reimbursement strategies set on a value-based principle, which depends not only on direct therapeutic effect, but also on patient compliance and adherence.

Insights gained from a better understanding of patient behavior will be vitally important—serving not only as validations for, but also playing a key role in, a treatment regimen itself. Exercise, mobility, social interactions, and behavioral patterns will play a greater role in determining whether patients perceive a sense of wellbeing, as opposed to just being told they are getting better. Understanding the mode of action at a chemical level is crucial, but understanding human nature and human behavior is often the key to determining in what situations a new treatment will actually work.

Patient outcomes combine collective and individual experiences, enabling clinicians to fast-track conclusions in the lab into everyday clinical

FIGURE 2: Number of New Drugs Approved by the FDA Compared to the Number of Filings, 1993 to 2016



Source: U.S. Food and Drug Administration

life. Companies will take this even further through accelerations in personalized medicine, recognizing that all human beings are different and that their characteristics, behaviors, and experiences shape wellbeing.

Data Currency in Clinical Trials

While clinical research continues to advance, the demand for better, faster, more effective treatments shows no sign of slowing. The kinds of scientific advancements that once took 10 years to reach the mainstream could soon take less than two years. To sustain this quest for better knowledge and more effective treatments, however, researchers need to better understand myriad *in vivo* and *in vitro* biochemical processes. That means connecting individuals across the globe—from patient to caregiver, from life sciences to healthcare organizations, and beyond—into the regulatory landscape. Data represent the unit of intelligence, currency, and commodity all wrapped into one neat package.

To establish a free-flowing data stream is difficult enough, but data alone do not deliver the end result. Data are ubiquitous and come in a wide range of volumes, varieties, and velocities. To successfully operate in a knowledge-based economy, data must be consumable and available in real time to derive actionable insights.

Today, the medical development industry is investigating the use of wearable devices, such as FitBit, Garmin, and many others—each capable of generating tens of millions of data points daily. Imagine combining those data with real-time observations, clinical assessments, long-term medical histories, financial data, behavioral data, and even social data. Exploring and characterizing patients from so many dimensions would enable clinicians to create a picture of each individual on a macro and micro level, from cradle to grave, from their very genetic beginnings to their current day experiences.

However, the data are not enough, nor is reviewing the data sources in isolation or combining the data into a periodic dataset. Companies will need to create a complete picture of the individual, refreshed every time a new data point is generated or recorded, in order to turn raw data into actionable insights and decisions. A direct line must be drawn between decision making and continuous improvement in patient wellbeing.

Pulling together this vision of an individual has another acute benefit. By sharing the outcomes and the characteristics of that individual, the industry can connect caregivers and patients across the globe, adding to the knowledge pool and advancing research in unimaginable ways. By mining data confidently, companies can find patterns and draw conclusions that have always evaded researchers until the very end of a clinical study, enabling real-time course corrections that reduce exposure to unnecessary treatments and redirect efforts to the best options available.

In parallel with clinical results, companies will also be able to seek operational patterns and identify problems, challenges, and obstacles faster. Many clinical trials still rely on manual, paper-based, or obsolete systems to collect, manage, and report clinical trial data. Time from event to analysis is still measured in weeks and months, when the need is for minutes and seconds. The application of first-generation eClinical platforms has been heralded as a big achievement, but these efforts have yet to accelerate clinical research or reduce the costs of research in any significant way.

In order to achieve a state of complete and concurrent data—with data equaling knowledge and knowledge leading to better decisions—data should be managed with a single software platform that empowers participants to optimize their contributions in the data value chain. The platform needs to create a coherent and contiguous environment for management of patient data, enabling research in all of its formats, through all of the contributors and consumers of those data.

A Better Way is Needed

EDC systems were first introduced 40 years ago for clinical data management, but really took off at the turn of the century. However, today's EDC is arguable still not a central, critical part of the clinical trial process. More often than not, clinical investigators still turn to paper and pen before EDC; while clinical trials are getting increasingly more complicated, technology is not being leveraged to simplify this complexity. If anything, it is common to find investigators bypass technology completely in favor of manual data capture and then input the data into EDC systems as an afterthought. Does this actually render today's EDC as unfit for purpose?

Let's explore that last question for a few moments, and consider the following stumbling blocks to widespread EDC adoption and making it core to clinical trials:

E for Electronic: Many EDC solutions are still reliant on the traditional paper-based processes, and most patient visits are recorded using paper and pen. These manual steps expose the entire clinical trial process to unnecessary risk and inefficiency.

D for Data: EDC Solutions are really electronic case report form (eCRF) tools that fail to address total data needs. In fact, eCRF data can easily represent less than 20% of study data, according to various estimates.

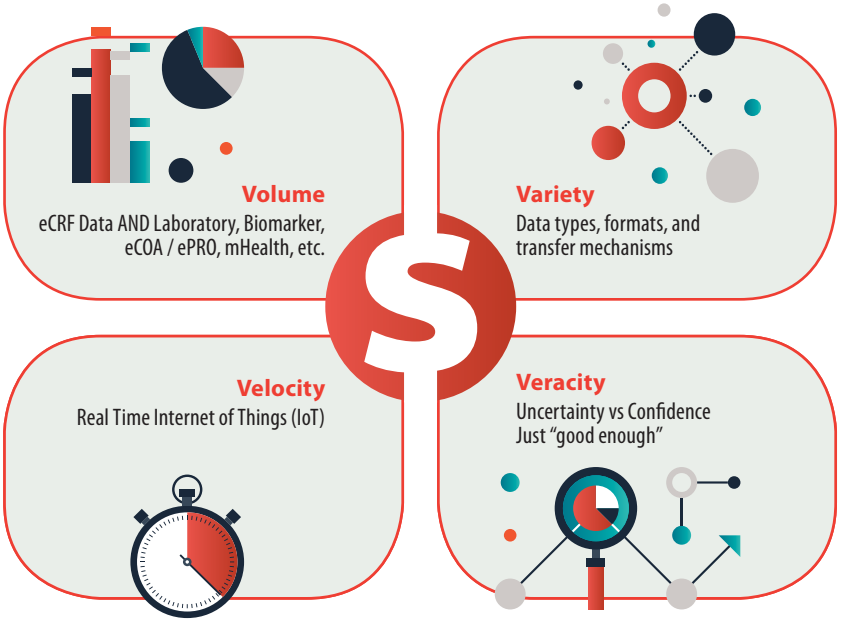
C for Capture: If all your EDC solution does is enable data capture, what about data management, monitoring, and reporting?

For clinical trial solutions to be classed as "fit-for-purpose," all of the incoming data must first be accessible in real-time and in one place. This provides a complete and concurrent view of data that is very specific to every patient, effectively creating a patient passport. A real-time window into patients' own worlds can deliver a better understanding of their symptoms, behaviors, and actions. Consolidating data not only advances the patient cause, but also improves the likelihood of success. Trials become faster, better informed, more knowledgeable, and better placed to react to whatever events arise.

Armed with heightened anticipation, patients don't buy drugs anymore, they buy outcomes. This means manufacturers will see their reimbursement strategies set on a value-based principle, which depends not only on direct therapeutic effect, but also on patient compliance and adherence.

Within pharmaceutical companies, the quest for understanding has accelerated, leading to the establishment of a knowledge-based economy with data as the currency. The more we know, the more we can develop these advanced solutions to not only meet, but get ahead of expectations.

FIGURE 3: Finding the Value in Data



To be fit for purpose, a data management tool (perhaps EDC) needs to address each and every data type plus the "four Vs" of data (see Figure 3):

- **Volume:** Managing vast quantities of data (structured and unstructured) without system performance degradation or financial loss. Today's EDC and eCRF solutions are designed to just manage data entered at the site, which is typically just a fraction of the total data in a study, according to various estimates.
- **Variety:** Managing data from a variety of sources, in differing formats and data types. Many EDC or eCRF solutions are designed to manage structured data, in limited format types.
- **Velocity:** Managing data in real time and consuming and supplying data with simplicity and elegance. EDC or eCRF solutions often are not designed to handle large volumes of data, so adding significant volumes causes severe performance delays.
- **Veracity:** Recognizing that not all data are born equal and that different strategies may be required for each data point (in essence, a risk-based data strategy). EDC and eCRF solutions are designed to manage data by type, and therefore need external assistance to drive more varied strategies.

Advanced, fit-for-purpose EDC solutions will address the needs for volume, variety, velocity, and veracity, and will lead to a full value assessment that aids study design, execution, and conclusion.

By mining data confidently, companies can find patterns and draw conclusions that have always evaded researchers until the very end of a clinical study, enabling real-time course corrections that reduce exposure to unnecessary treatments and redirect efforts to the best options available.

Realizing the Clinical Trials of the Future, Today

The life sciences industry will, very soon, be able to eliminate the need for paper in a clinical trial setting. However, companies need to not just eliminate paper, but completely redefine user experiences to be *paperless*—electronic systems will no longer be designed to look and behave as pieces of paper. This will result in user interfaces that are far more intuitive and that have advanced functionality, such as search and automatic grouping, designed into the system.

Real progress will also come from tackling data at the source. More often than not, source data are still recorded on paper manually with a pen or a paper-like format (using Microsoft Excel or Word). The resultant need for source data verification has a significant negative impact on the ability to reduce trial time or cost, and has been subject to many recent reviews that highlight only minimal quality advances.

As patients record more of their own data, paper is still the preferred solution. This only exacerbates and extends traditional challenges. For example, the "car park syndrome" is well documented, with patients who forget to fill out their diaries or questionnaires trying to recreate their experiences and symptoms as they sit in their cars just before they walk in to see their doctors. If company leaders tackle the source data challenge correctly, they not only advance clinical research, they also create a path to better, faster, long-term medical records that facilitate data sharing across multiple solutions (i.e., EDC and electronic health records).

While cloud-based technology and Big Data management have delivered proven results across the board in all industries, the life sciences industry has been slow to adopt a true cloud-based solution capable of delivering on global usage, minimizing costs, and handling data. Mainly, this is due to the lack of a true cloud solution that addresses these issues to date; when software doesn't work, it makes routine tasks and processes more difficult.

The Next Wave of Innovation in Clinical Data Management

Clinical trials are a very patient-centric, patient-driven process. Someday soon, patients will have complete control of their data. Personalized medicine is designed to ensure that our research delivers medical solutions that are better defined and that increase an individual's likelihood of responding. To understand individuals, each patient must

be closely examined, including through the use of data that haven't yet been considered for clinical trials. The true fit-for-purpose EDC solution will handle all of the data a patient can generate, and use those data to derive real-time decisions for patients and caregivers.

Clinical research can become truly global, connecting patients and caregivers across the globe. This opens up new vistas for clinical data capture and management to bring the trial to the patient. The Internet-of-things (the interconnection via the Internet of computing devices embedded in everyday objects, enabling them to send and receive data), for example, has increased the ability for data to be shared in real time and opened up the possibility of integrated data from varied sources flowing into clinical trial management. With it, the industry can take clinical research to previously improbable, if not impossible, places. Consider, for instance, rather than sites finding only patients who live or can temporarily stay nearby, how it may soon be a routine situation in which patients can remotely find trials based anywhere through smart devices and the experimental drugs can be administered and monitored from thousands of miles away.

Further, while succeeding quickly is a critical goal, failing early in trials is also vitally important for both financial and patient wellbeing reasons. Not every new clinical solution will drive benefit, therefore, there is opportunity to redirect money, resources, and patients.

Cloud computing, mobile health technology, Big Data, and the Internet of things hold immense potential when it comes to transforming clinical trials, especially ones that span geographic boundaries. A global, cloud-based solution for clinical data management makes installation, ongoing maintenance, and performance inherently easy, while managing cost, time, and resources. The true, fit-for-purpose EDC solution will work anywhere, anytime, and enable life science companies to design and execute the trial that they want, not the trial that is limited by technology today.

As important, this type of Internet-enabled cloud solution will increasingly support a global economy, including emerging and developing countries where 54% of adults identified themselves as Internet users in 2015.[3] Of course, the digital divide remains a challenge, but as more tech giants like Google (with its "Project Loon" initiative) and Facebook (with its "Internet.org" initiative) drive innovations forward to bring the Internet to more people, this challenge will slowly, but certainly, diminish.[4]

Conclusion

The life sciences industry is at an inflection point where the drive for patients, treatments, and research is increasingly global, medicine is becoming personalized, and there is a growing demand for new drugs to reach the market faster. With these trends in mind, a true cloud-based clinical data management solution that delivers global clinical trials and incorporates a high variety, volume, and velocity of data into personalized clinical trials is needed. This system will go far beyond the EDC solutions of today, which have not delivered on innovation in well over a decade, as well as beyond the eCRF limitations that have historically governed clinical trial processes. Clinical trials are still largely paper-based undertakings, and EDC systems serve largely as data entry systems.

The next generation of EDC solutions will combine data from every source in real time, present those data to all consumers, and facilitate clinical trials. This will mean embedding technology across the clinical trials process—from patient to regulator—ensuring that every observation, result, and event is captured as it occurs. Currently it is typical for data to be recorded on paper first and entered many days later. Ideally, however, data will be digitized at the source precisely when a patient event is happening, anywhere in the world, at any time, and will become a part of the global dataset immediately, not days or weeks later. Learning, patient management, and ability to address challenges will all happen in real time.

Technology will not only support the clinical trial, but the wider healthcare systems, feeding data into the patient's long-term medical records. The benefits of harmonizing across life sciences and healthcare will reap huge rewards, and will ultimately save the need for some research altogether. Still, the life sciences industry has a long way to go when it comes to leveraging technology to transform clinical data management. Industry is moving fast toward digitalizing clinical trials on a global scale, and the life sciences companies that are not quick to ride this change will soon be left behind with insurmountable costs, unable to keep up with the changing economy.

To change clinical research is to change patients' lives, and the power to do this comes from encouraging fresh innovations and identifying the barriers that stop our advancement. Data and knowledge help us to learn, and it is through learning that we can make real change.

References

1. U.S. Food and Drug Administration. Understanding Generic Drugs—Facts About Generic Drugs. www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/ucm167991.htm
2. Drugs.com. Looking ahead: pharma projections for 2016 - & beyond. https://www.drugs.com/slideshow/looking-ahead-pharma-projections-for-2016-and-beyond-1230
3. Poushter J. 2016. Pew Research Center. Smartphone ownership and internet usage continues to climb in emerging economies. www.pewglobal.org/2016/02/22/smartphone-ownership-and-internet-usage-continues-to-climb-in-emerging-economies/
4. Glick H. 2015. Global Citizen. Google wants to deliver internet to the developing world—via balloon. https://www.globalcitizen.org/en/content/google-wants-to-deliver-internet-to-the-developing/

Richard Young (richard.young@veeva.com) is vice president for Vault EDC with Veeva Systems and a former vice president of global consulting partners for Medidata Solutions.

Ensuring Compliance with Part 11: *A Site's Perspective*

PEER REVIEWED | Cristina Ferrazzano Yaussy, MPH, CCRP | James Wetzel

[DOI: 10.14524/CR-17-0005]

Today's clinical research sites are under tremendous pressure to produce more in an increasingly complex environment; however, the sophistication of sites' information technology (IT) systems often remains antiquated, lagging those used by the healthcare organizations with which they work. Office bookshelves bursting with paper binders function better as cubicle walls than workable repositories. Manual processes limit credentialed staff from realizing potential, and siloed systems and departments prevent productive collaboration.

In this environment, as more sites are looking to implement technology to go paperless, improve standardization, and provide secure access to essential documents, site staff's experience with ensuring compliance with 21 CFR 11 (Part 11) of the *Code of Federal Regulations*—focusing on the U.S. Food and Drug Administration's (FDA's) standards for electronic records and electronic signatures—may be limited. Balancing the need to maximize efficiency and ensure compliance presents a challenge, but with the right resources, the challenge is an achievable one. Gaining a better understanding of the purpose, scope, and components of Part 11 will help sites achieve their compliance goals.

Understanding Part 11: Purpose & Scope

In light of the Paper Reduction Act of 1995, the FDA aimed to rid itself of inefficiencies in record keeping. Recognizing the value of computer systems, yet the need to balance the security, authenticity, and reliability of electronic records, the FDA set forth to define regulations that would allow for the use of electronic records in the agency's mission. Thus, Part 11 was released in 1997.

Part 11 plays a vital role in the larger purpose of the FDA. By ensuring the security, authenticity, and reliability of data collected during a trial—and the systems that manage and process those data—the agency aims to ensure the safety and protection of the public.

Much debate has ensued over the applicability of the regulation, largely due to a lack of understanding. Essentially, Part 11 applies to any organization engaged in FDA-regulated research that maintains records electronically. This includes any records in electronic form, whether created, modified, maintained, archived, retrieved, or transmitted to others.[1] The general rule is that if a record is sent to the FDA or is required by the FDA to be maintained, and is managed electronically (electronically signed, disseminated, stored, etc.), it falls under the regulation.

Understanding Part 11: Five Components

Developing a process for Part 11 compliance at a research site can be a good thing. More often than not, it becomes an opportunity to look at the site's internal processes, the state of its standard operating procedures (SOPs), the presence or lack of a quality management system, and its ability to entertain inspections and audits. Furthermore, addressing the expectations of Part 11 thoroughly better prepares a site for the technologies of tomorrow.

The development of a site's Part 11 compliance process can be broken down to five main components, as described in the following sections.

Define Policies and Procedures

The first step to building out a Part 11–compliant process is to have a solid foundation and appropriate guidance, policies, and SOPs.[1] SOPs demonstrate

LEARNING OBJECTIVE
After reading this article, participants should be able to understand and identify critical components related to 21 CFR 11 compliance and how to implement and maintain an effective compliance process.

DISCLOSURES
Cristina Ferrazzano Yaussy, MPH, CCRP;
James Wetzel:
Nothing to disclose

a commitment to quality and reinforce the operational practices that a site upholds. They also serve as a resource for training staff, so that research teams understand their roles in following procedures and maintaining compliance with Part 11.

As a best practice, sites should maintain a portfolio of SOPs (see Table 1). This will help facilitate a consistent approach to implementing technology and safeguard against any potential oversights of the critical components of Part 11.

When moving to a document management system, sites should determine in advance which record(s) will be maintained in electronic format and document this decision in an SOP. Should a sponsor, monitor, or auditor inquire about such procedures, a well-developed SOP will ease their concerns.

System Functionality Review

When selecting a system to manage electronic documents and signatures, sites should conduct a thorough review, as specific functionality is required under Part 11 (see Table 2). This review should not be limited to the minimum required functionality, such as audit trails and authority checks; sites should use this as an opportunity to evaluate how the system can impact other site operational areas.

Consider, for example, the general auditability and configurability of the system. Does the system provide advanced keyword search functionality, so that documents are easily retrieved by staff or reviewers who are unfamiliar with naming conventions or file structures? Inadequate accessibility or retrievability can impede the auditing process, which could lead to inspection findings. Furthermore, files that are organized, secure, and readily accessible will improve overall staff efficiency.

Can the system be configured or modified by administrators without requiring time-consuming revalidation? For example, you hire a new regulatory specialist and need to modify the system to allow access to regulatory documents, but not financial documents. A well-designed system can accommodate these types of administrative changes without requiring revalidation (explored further below). Furthermore, it will help a site to accommodate growth without needing to rely on the vendor for every modification.

Site leaders will want to decide if they desire a system with advanced access functions that allow administrators to control whether certain users can upload and edit documents, but others only to view and sign those same documents (or not see them at all). Robust access controls and permissions can allow for a more controlled, yet more collaborative team.

While the software manufacturer can provide guidance in this review, it is the responsibility of the site to conduct and document a review of the system's functionality as it relates to Part 11. Use the system review as an opportunity to learn how the system can impact overall efficiency and usability.

Vendor Selection: Finding the Right Partner

Similar to an FDA inspection of a site, a site's evaluation of a vendor provides insight into the vendor's development and quality management processes. As vendors are entrusted with site data, site leaders should ensure they have adequate controls in place to prevent issues and handle exceptions.

Furthermore, auditing a vendor facilitates constructive dialogue between the site and vendor,

TABLE 1: EXAMPLES OF STANDARD OPERATING PROCEDURES (SOPS)

SOP	Description
SOP Development and Maintenance	Outlines the process by which all other SOPs are developed, approved, and maintained
Vendor Selection/ Audit	Outlines the procedures of performing vendor audits to ensure software providers are selected based on their capability to provide quality software and documentation for system validation
Records Management	Outlines how and by whom documents will be managed, including matters related to certified copies, retention, and accessibility
Software Implementation and Maintenance	Outlines initial validation, user acceptance testing (UAT), ongoing maintenance, and change control procedures
Electronic Signature Policy	Attests that users understand that their electronic signature holds them accountable; a letter of Non-Repudiation Agreement for digital signatures must be submitted to the FDA prior to change[3]
Training	Ensures users have adequate training and agree to terms of using the system

TABLE 2: CRITICAL COMPONENTS OF PART 11 FUNCTIONALITY

System Feature	Part 11 Compliant Application
Electronic Records Management	• System designed for electronic records management and functions as designed • Records are available for export and review throughout the retention period • Workflow follows sequential steps and prevents nonsequential actions
Audit Trail	• Automatic tracking of changes to electronic records • Date and time stamp for all actions and changes • Audit trail available for review and export throughout retention period
Security	• Access controls based on user role or permissions • Prevention of unauthorized access • Alerting of unauthorized access attempts • Secure access/password reset methods
Electronic Signatures	• Automatic tracking of name, date, time, and Statement of Testament associated with signature • Viewable and exportable manifestation of eSignature with Statements of Testament • Executing and linking the signature to the underlying record • Signatures cannot be attached to other record or removed

Balancing the need to maximize efficiency and ensure compliance presents a challenge, but with the right resources, the challenge is an achievable one. Gaining a better understanding of the purpose, scope, and components of Part 11 will help sites achieve their compliance goals.

which can lead to improvements in product quality. Poor development practices can lead to performance issues resulting in lost time (e.g., recovering information) and money (e.g., to purchase another system), damage to data integrity, and exposure to gaps in compliance with Part 11 or SOPs.

Sites should review the vendor's SOPs related to training practices, servers, records retention, disaster recovery, and software development/validation. This will provide insight into the vendor's development practices, as well as its understanding of the requirements of Part 11.

Evaluating the vendor's implementation and software release (or update) process is also important, as this will play a key role in ongoing maintenance and stability of the system. System updates are necessary for ongoing security and functionality improvements. However, if updates are released hastily or without adequate notice from the vendor, a site may be unprepared to perform adequate testing or training. Conversely, if updates are infrequent, desired improvements in functionality will not be met and known problems or "bugs" can perpetuate unreliable records.

If a site has an IT department, that department's staff should be involved in the process from the very beginning. Not only will they provide insight from a technology perspective, but they may also need to work closely with the vendor to ensure their procedures or requirements can be met. Sites without dedicated IT support should look for a vendor that provides additional assistance.

Sites should also closely review the level of support the vendor will provide for training and ongoing validation. Without adequate support, a site will need to plan for additional time and expertise in these areas. In the larger sense, a vendor that is knowledgeable and dedicated to Part 11 compliance can function more as a partner by ensuring a smooth transition and long-term success.

Validation

The process of performing and documenting systematic testing (validation) of the system is also a critical component of compliance with Part 11. In the same manner a car manufacturer may conduct a crash test to ensure the airbags work, sites must test their systems to ensure they function reliably. As we increasingly trust systems to perform tasks, we must ensure they perform them correctly.

While validation can be a complex chore, industry trends point to an increased focus in this area. In fact, the November 2016 revisions to the International Council for Harmonization's (ICH) Guideline for Good Clinical Practice E6 (R2) specifically require that computer systems be validated.[2] This requirement was developed to offset sites' increased reliance on allowing sponsors, contract research organizations (CROs), and vendors to conduct validation on their behalf.

While a qualified and knowledgeable partner can help, ultimately, validation is the responsibility of the site. It is not a one-time occurrence or something that is "covered" by a vendor or sponsor—it is an ongoing process that sites need to own.

To conduct system validation, sites should develop a user acceptance testing (UAT) protocol to systematically evaluate performance. The UAT protocol should outline what the system should do (requirements), how it should do it (specifications), and how testing should be performed to ensure it functions correctly. The results should be documented along with any unusual observations. UAT should be repeated (revalidation) when requirements and specifications relating to Part 11 are modified, which typically happens with a major system update.

Similarly, validation of the infrastructure (hardware) hosting the system must also be conducted. The process may change whether the system is hosted by the site or by the vendor. However, the responsibility of ensuring the integrity of the hardware ultimately falls on the site. When using a vendor, a site is entrusting the protection of its information in the vendor's hands, therefore the site should ensure the hardware being used to host its data is properly validated.

Training

Training is an integral part of selecting and using electronic systems for research projects. The processes surrounding how and when training is conducted and documented is a responsibility of the site that can be made more efficient with assistance from vendors. Simply put, persons who develop, maintain, or use electronic records and electronic signature systems (staff for vendors and the site end-users) must have procedures in place so that they have the proper education, training, and experience to perform their respective tasks.

Training is everyone's responsibility, and is necessary to ensure that the system is used properly and that users can identify when it may not be working correctly. Inadequate training may lead to compliance issues, as data integrity and access controls can be compromised through misuse of a system. Training should be conducted upon implementation and updated along with any major changes to the system that follow.

As an added level of support to sites, and to help promote compliance with Part 11, a system can offer automated training to all individuals upon entry and request that they attest to understanding their responsibilities for documentation purposes. Training should be consistent with the function/responsibility of the end-user, and should be documented along with the eSignature attestation. This attestation is to document that users understand that when they use a system and apply their eSignature, it is equivalent to their hand-written signature, which is a fundamental aspect of Part 11.

Where Do You Start?

So, how do research site staff begin to tackle Part 11, especially if they are questioning if it will even be worth the effort? Besides pleasing an auditor, what benefits will a site realize from compliance with this regulation? Moreover, where does one begin, given the volumes of information about Part 11 that a simple Google search provides?

Some site leaders may even question if, in the event of an FDA inspection, the agency is really going to look at Part 11 compliance—especially given that there have been few if any inspection findings to-date of research sites nonconformance in this area. The concerns are valid, but consider the following: Recent FDA guidance on investigator responsibilities highlights an increased focus on the research site. In fact, the aforementioned ICH E6 (R2) references many of the same concepts outlined in 21 CFR Part 11 as they relate to the investigator's responsibilities for data handling, record keeping, and audit trails. Further, the increased use of technology systems to manage essential documents means these systems are more likely to be looked at closer by auditors and inspectors.

The best place for site leaders and staff to start is to evaluate what they don't know about Part 11. Know when a function falls under compliance and when validation should occur. At a minimum, know that it is not a "task" to be relegated to the IT team, nor is it a product feature to be bought or a box to be checked. While others can certainly help, maintaining compliance is an operational process whose responsibility is shared throughout the site.

Next, take inventory of what needs to be done. One critical question that needs to be asked early on is "What can we improve as a site before, during, and after this compliance effort?" Perhaps new SOPs need to authored? Responsibilities need to be better defined. Online shared drives need to be organized. Make a list.

Next, evaluate how current processes and procedures may be impacted. How might this affect staff onboarding? Does the site have specific training requirements? Does it have specific back-up or retention requirements that are different from what vendors provide?

Also evaluate the capabilities of everyone at the site to carry out these tasks. How will this affect new staff? Is it a large site with a dedicated training or validation team? Or a small site with stretched resources? Take stock of where help may be needed.

There is an abundance of resources at sites' disposal for assisting with complying with 21 CFR Part 11; whitepapers, websites, federal regulations, case studies, vendors, consultants, and even CROs and sponsors can be a resource for learning the steps involved. Do not be afraid to lean on vendors or reach out to CROs and sponsors, but most importantly, find a resource that has successfully navigated these compliance waters.

After the validation and compliance efforts have been completed, understand that it is a journey and not a destination. Documentation of ongoing efforts of compliance, making use of a quality system, documenting and doing what your SOPs say—these are all part of the process.

In summary, then, the following is a high-level view of key considerations for implementing a Part 11 compliance process:

- Perform a self-assessment and gap analysis
- Identify how to fill in the gaps
- Develop policies and procedures
- Find a solution and a knowledgeable partner to fill gaps
- Implement new processes
- Implement and validate the system
- Train your team
- Perform ongoing evaluation and quality assurance

Once site staff have undertaken the process and received feedback on their efforts (hopefully through something other than an FDA Form 483), they will be equipped to apply the process to new technologies that require compliance. Additionally, sponsors and CROs will recognize the site's new-found level of sophistication and be more likely to want to conduct studies at the site.

Conclusion

One of the greatest challenges facing clinical research sites is ensuring regulatory compliance, especially when using technology to manage documentation. While not easy, the journey to compliance can improve the research site in more ways than just in terms of its validation and audit preparedness; it can bring better SOPs, happier staff, and more efficient research conduct.

References

1. U.S. Food and Drug Administration. Part 11 of Title 21 of the *Code of Federal Regulations* on Electronic Records; Electronic Signatures—Scope and Application. https://www.fda.gov/RegulatoryInformation/Guidances/ucm125067.htm
2. ICH Harmonised Guideline. 2015. Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2). https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Addendum_Step2.pdf
3. U.S. Food and Drug Administration. Electronic Submissions Gateway—Appendix H: Letters of Non-Repudiation Agreement. https://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/ucm113964.htm

Cristina Ferrazzano Yaussy, MPH, CCRP, (cristina@complion.com) is vice president for professional services with Complion, Inc., in Cleveland, Ohio

James Wetzel (jwetzel@okheart.com) is a senior director at the Oklahoma Heart Hospital.

Using EHR Data Extraction to Streamline the Clinical Trial Process

PEER REVIEWED

Jennifer Stacey | Maulik D. Mehta, MBA

[DOI: 10.14524/CR-17-0004]

Since 2005, the average time from approval by the U.S. Food and Drug Administration of an Investigational New Drug application to a New Drug Application approval has been 8.1 years. From 2003 to 2013, the cost to develop an approved new drug has more than doubled from more than $1 billion to nearly $2.6 billion.[1]

Much of the cost and slowness of the overall process is a result of difficulties in recruiting appropriate patient populations. Recent research shows that only 13% of investigative sites exceed their enrollment, and that initial Phase II–IV study timelines are often doubled to reach study enrollment goals.[2] This has resulted in unnecessary protocol amendments that cause delays and dramatically increase costs of developing new therapies.

The three main players in the clinical trial process—biopharmaceutical firms, contract research organizations (CROs), and healthcare organizations—face obstacles as they navigate through the difficult waters of bringing new drugs to market. For instance:

- **Biopharmaceutical firms** lack real-time data, so site selection is often relationship-driven and susceptible to site failures. Clinical investigators are prone to overestimation of patient availability, which leads to under-enrolled study sites. Overly restrictive eligibility criteria, among other trial characteristics, also make some protocols unfeasible.

  Further, protocol amendments pose one of the greatest obstacles to effective clinical trial execution. Amendments are costly, time-consuming solutions to underlying clinical trial issues such as increasingly complex protocol design and difficulty recruiting patients. Nearly two-thirds of protocols require at least one substantial amendment, and a typical protocol ends up with an average of 2.3 amendments. On average, the cost of a single protocol amendment is $453,932 and the total cost for sponsors to implement "avoidable" protocol amendments is nearly $2 billion annually.[3]
- **CROs** are challenged when inclusion/exclusion criteria are chosen without verifying the impact on availability of a cohort, which can create avoidable amendments. The possibility of underbidding the project also increases their risk. CROs strive for competitive differentiation, but the lack of tools to leverage clinical and health-related data can be a barrier to winning more business. CROs endeavor to help their pharma clients develop more pragmatic operational solutions, but require real-world data for better protocol design and feasibility studies.
- **Healthcare organizations** seek to attract more clinical trials—both to generate additional revenue and to help develop new therapies. Unfortunately, competition is increasing for a shrinking pool of National Institutes of Health (NIH) funding and grant funding rates in general are declining. The number of newly registered NIH-funded trials decreased 24% from 2006 to 2014. At the same time, competition from new research areas has increased.[4]

LEARNING OBJECTIVE
After reading this article, participants should be able to discuss the benefits of utilizing EHR technology in planning and conducting clinical trials.

DISCLOSURES
Jennifer Stacey;
Maulik D. Mehta, MBA:
Employee of TriNetX, Inc.

Increasingly, the answer is to extract real-time patient clinical data residing in healthcare organization electronic health records (EHRs). Leveraging these detailed data allows pharma companies and CROs to identify patients who match exactly the eligibility criteria for the cohort they are seeking.

EHR Data are Key

The traditional clinical trial process is broken. The question is how to utilize technology to optimize the process.

Increasingly, the answer is to extract real-time patient clinical data residing in healthcare organization electronic health records (EHRs). Leveraging these detailed data allows pharma companies and CROs to identify patients who match exactly the eligibility criteria for the cohort they are seeking. EHRs are transactional systems, optimized for capturing and quickly retrieving individual observations about single patients.

Combing through individual records to find groups of patients is something most forms of EHRs do not support well, if at all. The class of software tools designed to identify patient cohorts relies on data extracted from EHRs and transformed to allow nimble cross-patient searching. The data "liberated" from EHRs frequently represent a subset of all available patient information, are typically limited to observations stored as discrete elements, and are therefore easy to extract.

Cohort identification tools use the extracts of data to provide a first pass at defining patient cohorts that match the criteria of interest. These cohorts are "coarse," and require additional refinement. Nonetheless, cohort identification tools eliminate the need to "boil the ocean" to find the specific patients required by significantly narrowing the target population to be reviewed, screened, and eventually enrolled into a trial.

A data-based approach reduces overall site attrition and results in fewer sites with more applicable patients. Ultimately, it will decrease the overall cost and accelerate the development of new drug therapies.

Emerging Enabling Technology

Some providers are already using healthcare information technology (IT) solutions to conduct clinical trial design and site feasibility studies. Although many of these data analytic offerings provide access to large patient populations, these solutions (e.g., data aggregators) are typically based on centralized data sets in single institutions.

For example, the Case Comprehensive Cancer Center at Case Western Reserve University in Cleveland, Ohio has developed an automated tool that matches patients with ongoing clinical trials at the point of care. Using this tool, physicians were able to facilitate patient enrollment in active clinical trials in conjunction with existing clinical workflows.[5] This ability to find the types of patients that exactly meet trial criteria quickly and easily illustrates the benefits of EHR data extraction technology.

Success in single institutions highlights the power of extracting and leveraging EHR data. The key to industry-wide success, however, is expanding this enabling technology to include larger databases collected from multiple healthcare organizations, broadening the scope of data they make available (e.g., biomarkers, imaging, information "locked" in narrative text of notes and reports, etc.), and increasing adoption of these tools across the spectrum of the biopharma research enterprise.

The nearly universal adoption of EHR technology, maturing standards and interoperability, a desire to use accumulating clinical data to improve care delivery, and growing appreciation that data collaboration is ultimately required to realize its full potential have opened the door to the widespread sharing of EHR data that represents the next step in improving the clinical trial process. Up to now, there hasn't been a real-time patient data resource available to help develop protocols and recruit patients. Pharma companies have been forced to use epidemiology data, which are often several years old or worse before being published, and may no longer be relevant.

Technology solutions now allow pharma companies and CROs to access EHR data from healthcare organizations globally on a near real-time basis. Advances have made it possible to study patient data securely. Companies can query de-identified, federated databases to research actual patients by reviewing aggregated EHR-based patient records. They can alter eligibility criteria, instantly see the effect on their overall cohort, and learn whether relevant sites have access to sufficient number of eligible patients. They also can identify problems with inclusion/exclusion criteria earlier during protocol development, significantly reducing the cost and delays caused by protocol amendments.

This new technology protects patient privacy by providing de-identified data during research, then allowing re-identification only after a healthcare organization has agreed to participate in a trial. This greatly improves the recruitment phase of the trial process.

Success in single institutions highlights the power of extracting and leveraging EHR data. The key to industry-wide success, however, is expanding this enabling technology to include larger databases collected from multiple healthcare organizations.

The cost to access a user-friendly EHR platform may strain the budgets of many small pharma companies or CROs, but affordable pricing models are becoming available to address this issue.

A Few Words of Caution

However, while EHR data offer many advantages to clinical research, some downsides exist. Extreme diligence is required to shield sensitive protected health information from cyber breaches, some data types may be missing from a given EMR, and coherent, consistent policies and practices for secondary use of EHR data need to be developed worldwide.

Further, the cost to access a user-friendly EHR platform may strain the budgets of many small pharma companies or CROs, but affordable pricing models are becoming available to address this issue. Despite concerns with EHR usage in clinical research today, the advantages of using this "big data" still outweigh these few current drawbacks.

Mapping Disparate Data to Enable Collaboration

A core element of cohort identification based on federated databases of EHR data is the mapping of disparate clinical data coding standards to a common terminology for ease of use and seamless research collaboration. This eliminates the need for healthcare organizations, pharma companies, and CROs to struggle with translating coding language from multiple systems and organizations.

Clinical data captured by EHRs and extracted for cohort identification is typically coded, meaning that individual data elements are assigned codes from relevant controlled terminology, or coding systems like ICD-10-CM, ICD-10-PCS, and CPT. Some data elements, while coded, are used under different standards at different organizations (i.e., providers of medication standards include Walters Kluwer's Medi-Span, Cerner's Multum, First DataBank, and others).

To provide interoperability, disparately coded data must be mapped to a unified set of standards. The mapping process can be costly, since current standards are at different stages of maturity and have varying levels of support and relevant tooling for mapping. A typical mapping exercise requires extensive manual review by terminology experts to ensure high quality. In addition, every mapping is dynamic, in that the effort requires ongoing maintenance due to changes in both the underlying source data and the target standard terminology.

In short, harmonizing data to a unified set of standard terminologies is a necessary step in enabling the functions of cohort identification tools and is a key feature of the new technology.

Using EHR Data to Avoid Costly Amendments

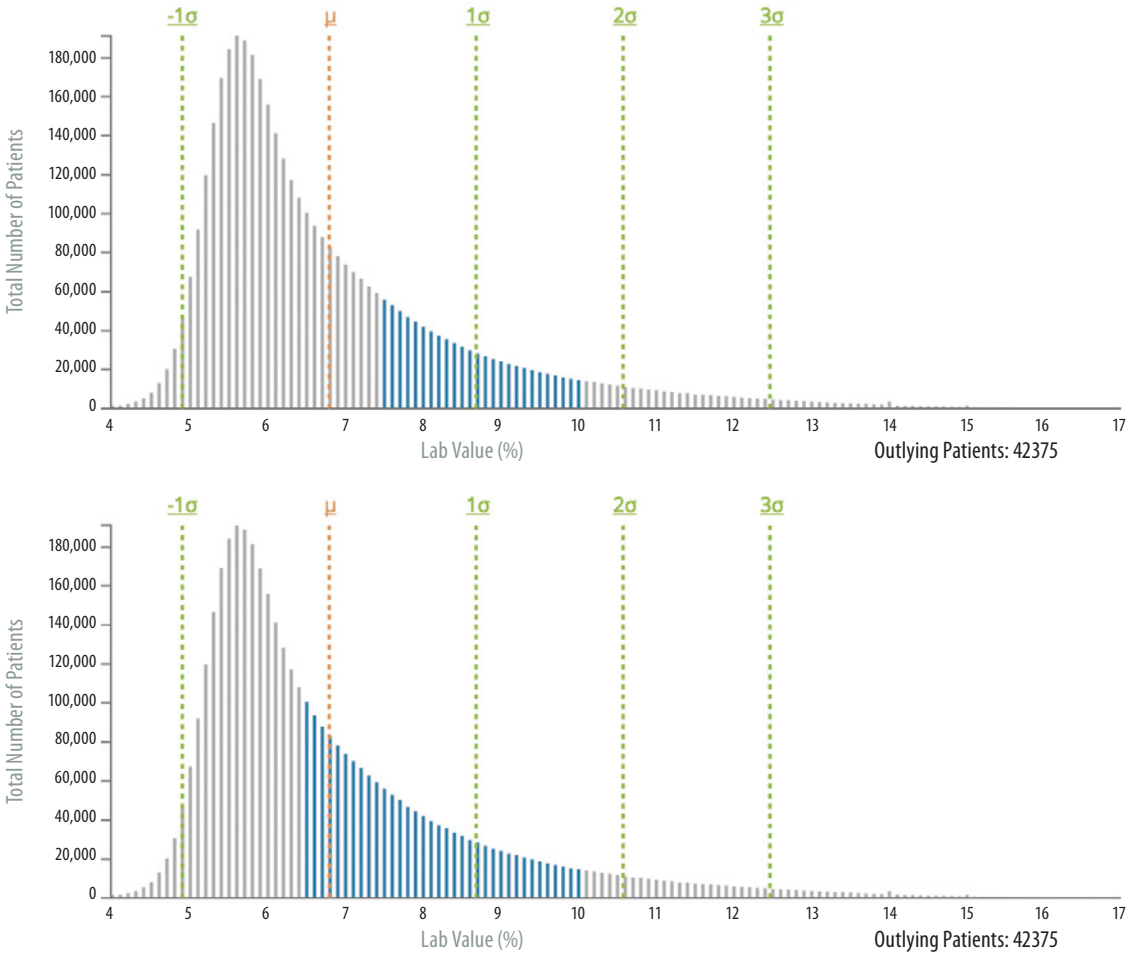
Some organizations have already begun using federated EHR data from multiple healthcare organizations to develop their protocols and recruit patients, and early results are encouraging. Planners, investigators, protocol writers, and strategy teams have been able to move recruitment planning upstream to align with the clinical design process. This has helped to ensure trial feasibility and reduce the number of preventable clinical trial amendments.

ICON, a CRO based in Ireland, was able to leverage EHR data from a global research network to support a bid defense for a European pharmaceutical company. The firm had been initially dropped from consideration, but was later able to become a viable contender because of its use of real-time EHR data.

At the bid defense, ICON presented an HbA1c sensitivity analysis, as the client was contemplating changing the lower range of its protocol from 7.5 to 6.5. Using the cohort identification technology, ICON was able to quickly run the analysis at both 6.5 and 7.5, and found that the difference in the number of matching patients was only 30 for that specific cohort (see Figure 1). Since the cohort already had more than 8,000 matching patients, ICON recommended that the client keep the study entry criterion at 7.5. Another CRO had advised changing the criteria, but the client was hesitant, as its entire program had been based on the 7.5 criterion. The client was pleased that ICON had been able to quickly provide real data from real patients to justify keeping the original higher threshold.

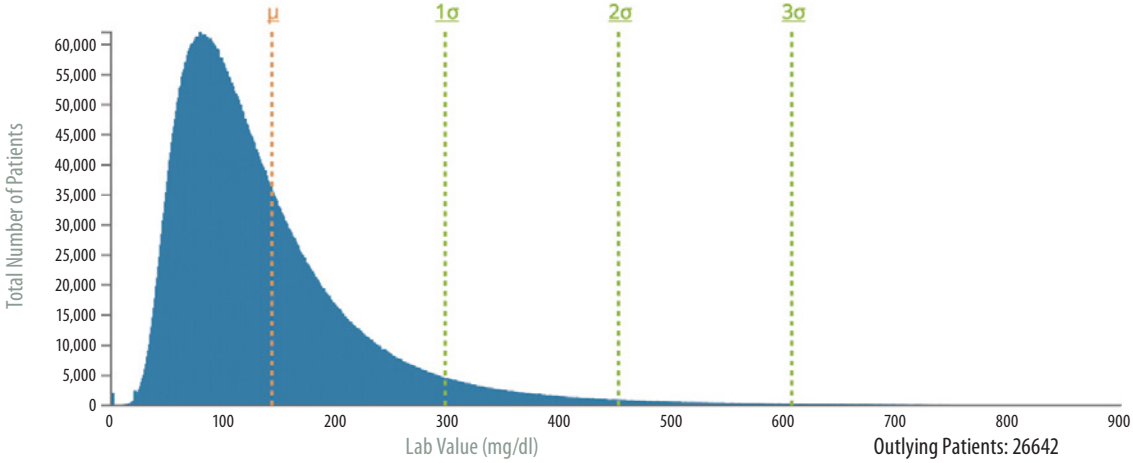
In another case, ICON was able to help a U.S. client determine triglyceride parameters to use as an inclusion criterion for a large cardiovascular trial being planned. In this situation, ICON, again using cohort identification technology, was able to show the full distribution of triglyceride lab results across a large representative population. It then adjusted the upper range so the client could see the effect on the patient population that still met the target cohort size (see Figure 2).

FIGURE 1: HEMOGLOBIN A1c SENSITIVITY ANALYSIS



A comparison of 6.5–10% vs. 7.5–10% HbA1c lab results. While the lab criteria alone yield a larger number of patients for the broader 6.5–10% range, the overall effect of modifying the lower range from 7.5% to 6.5% was negligible (less than 0.4% difference) when applied to the full study inclusion and exclusion requirements.

FIGURE 2: TRIGLYCERIDE LAB



A view of the number of patients according to their most recent triglyceride lab results. The EHR platform allowed the user to enter various value ranges to determine the best-suited triglyceride parameters for inclusion criteria for an upcoming study.

	Min	Max	Median	Mean(μ)	Std. Dev(σ)
Network Stats	0.0	20,957.0	113.00	143.37	154.44

Greater than or equal to mg/dl

Less than or equal to mg/dl

Most Recent Result Ever

FIGURE 3: ORIGINAL VS. EXPANDED AMENDED DISEASE CRITERIA

14,715 Patients
Population 5–17 years/any gender (7,127,901)

	M08 Juvenile arthritis
OR	L93 Lupus erythematosus
OR	M32 Systemic lupus erythematosus
OR	M33 Dermatopolymyositis (juvenile dermatomyositis)
OR	M34 Systemic sclerosis (scleroderma)
OR	M35.0 Sicca syndrome (Sjogren)
OR	M35.1 Other overlap syndromes
OR	M30 Polyarteritis nodosa and related conditions
OR	M31.3 Wegener's granulomatosis
OR	M31.5 Giant cell arteritis with polymyalgia rheumatica
OR	M31.6 Other giant cell arteritis
OR	M31.7 Microscopic polyangitis
OR	M31.4 Aortic arch syndrome (Takayasu)
OR	M30.1 Polyarteritis with lung involvement (Churg-Strauss)
OR	D89.1 Cryoglobulinemia
OR	L95.9 Vasculitis limited to the skin, unspecified
OR	M35.2 Beçhet's disease (Beçhet's syndrome)
OR	K50 Crohn's diseas (regional enteritis)
OR	K51 Ulcerative colitis

EHR technology allows for patient cohort size comparisons based on the addition of several diseases. In this example, an amendment that opened enrollment to patients with cerebral palsy, Duchenne muscular dystrophy, diabetes, celiac disease, or cystic fibrosis in addition to all other prior allowed diseases expanded the number of eligible patients by 72% within the 5–17 year age range based on target indications alone.

53,351 Patients
Population 5–17 years/any gender (7,127,901)

	M08 Juvenile arthritis
OR	L93 Lupus erythematosus
OR	M32 Systemic lupus erythematosus
OR	M33 Dermatopolymyositis (juvenile dermatomyositis)
OR	M34 Systemic sclerosis (scleroderma)
OR	M35.0 Sicca syndrome (Sjogren)
OR	M35.1 Other overlap syndromes
OR	M30 Polyarteritis nodosa and related conditions
OR	M31.3 Wegener's granulomatosis
OR	M31.5 Giant cell arteritis with polymyalgia rheumatica
OR	M31.6 Other giant cell arteritis
OR	M31.7 Microscopic polyangitis
OR	M31.4 Aortic arch syndrome (Takayasu)
OR	M30.1 Polyarteritis with lung involvement (Churg-Strauss)
OR	D89.1 Cryoglobulinemia
OR	L95.9 Vasculitis limited to the skin, unspecified
OR	M35.2 Beçhet's disease (Beçhet's syndrome)
OR	K50 Crohn's diseas (regional enteritis)
OR	K51 Ulcerative colitis
OR	G80 Cerebral palsy
OR	G71.0 Muscular dystrophy (Duchenne)
OR	E08-E13 Diabetes mellitus
OR	K90.0 Celiac disease
OR	E84 Cystic fibrosis

72% increase in eligible patient population

Some organizations have already begun using federated EHR data from multiple healthcare organizations to develop their protocols and recruit patients, and early results are encouraging.

FIGURE 4: ORIGINAL VS. EXPANDED AMENDED FRACTURE CRITERIA

1,018 Patients → 33,896 Patients

	532.0 Fracture of lumbar vertebra	45,596

The pharmaceutical company implemented another amendment to the same trial in order to expand the size of the potential patient population. In looking at only the fracture criteria, the initial inclusion criteria of vertebral fracture only identified 1,018 patients in the specified 5–17 age group, but it was augmented to 33,896 patients when all types of long bone fractures were later added—even with the requirement that they must occur in the prior two years. Our EHR source was able to show that the expansion of fracture criteria alone allowed a 97% increase in potential patients.

Event 2 – All of the terms in this event occurred between today and 24 months ago

	532.0 Fracture of lumbar vertebra	45,596
OR	542.2 Fracture of upper end of humerus	70,808
OR	542.3 Fracture of shaft of humerus	44,674
OR	542.4 Fracture of lower end of humerus	67,734
OR	552 Fracture of forearm	213,988
OR	572 Fracture of femur	92,469
OR	582.1 Fracture of upper end of tibia	44,436
OR	582.2 Fracture of shaft of tibia	65,717
OR	582.3 Fracture of lower end of tibia	28,856
OR	582.4 Fracture of shaft of fibula	58,482

FIGURE 5: ORIGINAL VS. FULLY AMENDED PROTOCOL CRITERIA ANALYSIS

20,513,595 – 18 sites	**Network**	20,513,595 – 18 sites
3,823,331 – 18 sites	**Population – Ages 5–17**	3,823,331 – 18 sites
8,565 – 17 sites	**Inclusion Criteria Diseases** *(plus all other remaining criteria)*	48,772 – 17 sites
2 – 1 site	**Allowed Fracture Types**	615 – 15 sites
0 – 0 sites	**Glucocorticoid Requirement**	38 – 7 sites

Using analytical tools available in our EHR source allows for comparison of the complete original (pre-amendment) protocol vs. the most current protocol (after several amendments). While the size of the EHR network and patients within the 5–17 age range remain the same in the top portion of both funnels, the impact of specific parameters—diseases allowed, types of fractures allowed, medication requirement—can be clearly noted in the resulting patient numbers. At the same time, the effect of all protocol criteria together can be considered. Here we are able to show that there were no potential patients who met the non-amended protocol criteria, while the fully amended protocol was broadened enough to identify 38 patients.

"Being able to use cohort identification technology based on EHR data provides us with the objective data and analytics on real patients to help our clients make decisions that matter," said Otis Johnson, PhD, MPA, vice president for feasibility and clinical informatics at ICON.

In an example of the technology's ability to drive in-depth portfolio planning, a leading pharma company was able to leverage a multisite federated EHR database to evaluate a long-standing inclusion screening criterion that was perceived to be hampering recruiting efforts. Using data extraction to research a larger population of quantitative data, the company was able to see from side-by-side comparisons with and without the criterion how it changed the eligible patient number. The company then removed the criterion from the protocol template, which improved the potential patient pool and recruitment efficiency to potentially avoid costly amendments.

Another global healthcare company using the traditional site and patient selection process ended up with five amendments over an eight-year period and enrolled a total of 23 patients. The initial protocol wasn't able to enroll a single patient. The study manager felt this would be the case, but had no tangible data at that time to dispute key opinion leaders who insisted there would be patients.

A retrospective analysis revealed how each amendment expanded the potential patient pool and delivered a collective assessment to the updated eligibility criteria overall. A final assessment that took all existing criteria and the five amendments into consideration and drew on EHR data from multiple healthcare organizations yielded 38 potential subjects. A similar analysis of the original protocol found zero patients—the same findings of the actual study before any amendments were considered.

As of the writing of this article, the trial has 23 patients enrolled, supporting the findings in the analysis and demonstrating the viability of EHR data analytics in "stress testing" a protocol for feasibility from conception to avoid costly amendments upstream (see Figures 3–5).

EHR Data–Based Results Match Epidemiologic Findings

The value of EHR-based studies has furthermore been validated in terms of ability to reproduce epidemiologic findings published in medical literature. EHR-based data extraction can provide a proactive method of producing accurately defined patient populations. This allows healthcare organizations, biopharma companies, and CROs to make better, more timely decisions.

Conclusion

Developing new therapies and getting them to market is cumbersome, time consuming, and costly. Flawed protocol design based on anecdote or opinions often fail to find the right patients for trials. Site selection based on art instead of real-world data is fraught with risks of trials closing due to failure to accrue patients. Cohort identification technology based on EHR data provides a better way.

The industry now has a treasure trove of real-time, relevant information in the form of EHR data being collected from nearly every healthcare organization. The key is getting to that information and leveraging it to make better upfront decisions and streamline the clinical trial process.

Along with the emergence of a culture of data sharing that improves availability of data for research, advances in data interoperability and maturing technologies for federated databases and cloud and data analytics are now allowing healthcare organizations, pharma companies, and CROs to tap into a vast wealth of data. As use of these collaborative networks increases, EHR data will soon become the key building block on which the industry can build a more effective, efficient process to bring new therapies to market faster. Eventually, that will lead to better clinical outcomes, which represent everyone's ultimate goal.

References

1. Getz K. 2015. The cost of clinical trial delays. https://www.ctti-clinicaltrials.org/files/pgct-session5.1-getz.pdf
2. Bachenheimer JF. 2016. Adaptive patient recruitment for 21st century clinical research. *App Clin Trials*. www.appliedclinicaltrialsonline.com/adaptive-patient-recruitment-21st-century-clinical-research?pageID=3
3. Getz K. 2011. Protocol amendments: a costly solution. *App Clin Trials*. www.appliedclinicaltrialsonline.com/protocol-amendments-costly-solution?id=&sk=&date=&%0A%09%09%09&pageID=2
4. Desmon S. 2015. Industry-financed clinical trials on the rise as number of NIH-funded trials falls. HUB (Johns Hopkins University). http://hub.jhu.edu/2015/12/15/industry-funded-clinical-trials-may-threaten-objectivity/
5. Sahoo SS, Tao S, Parchman A, Luo Z, Cui L, Mergler P, Lanese R, Barnholtz-Sloan JS, Meropol NJ, Zhang G-Q. 2014. Trial Prospector: matching patients with cancer research studies using an automated and scalable approach. *Cancer Inftcs*.

Jennifer Stacey (jennifer.stacey@trinetx.com) is director of clinical operations at TriNetX in Cambridge, Mass.

Maulik D. Mehta (maulik.mehta@trinetx.com) is senior vice president of TriNetX in Cambridge, Mass.

HOME STUDY HS

Technology for Trials

OPEN BOOK TEST

This test expires on April 30, 2018

(original release date: 4/1/2017)

OPINION: Data—The Foundation of Clinical Trials

1. **According to the author, which of the following will accumulate vast quantities of data, especially in clinical trials?**

- **A.** Reviewing data from long-completed studies and repeating those studies in new populations.
- **B.** Regulatory expectations that all data from human subjects be deposited with ClinicalTrials.gov.
- **C.** Increased use of personal fitness wearable devices by healthy persons enrolled as controls in studies.
- **D.** A greater understanding of the structures and behaviors that make up the human body.

2. **Recent patent expirations on top pharmaceutical products have led to which of the following?**

- **A.** A nearly 400% increase in the number of firms producing generic drugs since 2010.
- **B.** A loss of more than $120 billion in sales across a five-year period.
- **C.** Record numbers of patients being hospitalized due to use of prescription drugs for off-label purposes.
- **D.** A spike in adverse event reports from doctors seeing patients who've taken expired medicines.

3. **According to the author, what is required to turn raw data into actionable insights and decisions?**

- **A.** Data storage capacities that are unavailable to all but the largest pharmaceutical firms.
- **B.** Committees of reviewers representing both internal and external stakeholders.
- **C.** A complete picture of a patient, refreshed whenever new data points occur.
- **D.** Electronic data capture (EDC) systems with expanded capabilities that are still under development in the U.S.

4. **When were EDC systems first introduced?**

- **A.** 10 years ago
- **B.** 20 years ago
- **C.** 30 years ago
- **D.** 40 years ago

5. **Electronic case report form (eCRF) data are estimated to represent how much of total study data?**

- **A.** Less than 20%
- **B.** Nearly 30%
- **C.** More than 40%
- **D.** Exactly 50%

6. **What is necessary for clinical trial solutions to be classed as "fit for purpose"?**

- **A.** Data must be collected without error.
- **B.** Auditing must take place prior to entry into an EDC tool.
- **C.** All incoming data must first be accessible in real time and in one place.
- **D.** Outgoing data should have had two audits to ensure accuracy of source data.

7. **As described in the article in relation to data management tools, "variety" of data involves which of the following?**

- **A.** How expensive the data are to collect and mine.
- **B.** How many people involved in the study are allowed to input data.
- **C.** When to use risk-based strategies for collecting the data.
- **D.** What formats, sources, and types the data arrive in.

8. **How does source data collection using the paper format affect trials?**

- **A.** Increases time and costs due to need for source data verification.
- **B.** Decreases time and costs due to less equipment being required.
- **C.** Increases patient drop-out rates due to the "car park syndrome."
- **D.** Decreases site staff workload due to allowing the trial to close sooner.

9. **Which of the following happens when paper is used as the answer to data capture?**

- **A.** It provides ease of monitoring and auditing.
- **B.** It exacerbates and extends traditional data challenges.
- **C.** It reduces the need for usernames and passwords.
- **D.** It increases the likelihood of protecting data privacy.

10. **Personalized medicine is designed to do which of the following?**

- **A.** Ensure that research delivers medical solutions that increase an individual's likelihood of responding.
- **B.** Allow patients to choose what providers and procedures they would like to involve in their care.
- **C.** Streamline delivery of similar treatments across culturally similar patients with the same conditions.
- **D.** Cure patients of their diseases through the shortest and least expensive courses of treatment possible.

Ensuring Compliance with Part 11: A Site's Perspective

11. **Who must comply with 21 CFR 11 (Part 11)?**

- **A.** Only industry sponsors of clinical trials, as they are responsible for and initiate the clinical investigation.
- **B.** Any organization engaged in U.S. Food and Drug Administration (FDA)-regulated research that maintains records electronically.
- **C.** Any healthcare provider, including doctors and staff of clinics, hospitals, nursing homes, and pharmacies.
- **D.** Healthcare providers who conduct financial and administrative transactions electronically.

12. **Part 11 applies to which of the following types of records?**

- **A.** Only those that are sent to sponsors so that trial results may be published.
- **B.** Those that detail why a drug candidate was not approved for marketing.
- **C.** Records that are sent to FDA or required to be maintained by the FDA.
- **D.** All budget and contract records associated with the clinical trial.

13. **What are the key components for establishing Part 11 compliance?**

1. Establish site policies and processes
2. Evaluate the system functionality and audit the vendor
3. Validate the system and train all users
4. Obtain FDA approval for the system

- **A.** 1, 2, and 3 only
- **B.** 1, 2, and 4 only
- **C.** 1, 3, and 4 only
- **D.** 2, 3, and 4 only

14. **In selecting a Part 11–compliant vendor, which services should be provided for optimal success?**

- **A.** Initial system training for super users and fee-for-service support package.
- **B.** Ongoing training for all stakeholders and ongoing Part 11 validation support.
- **C.** A Part 11–ready system with a user manual and no additional support.
- **D.** Off-the-shelf system with suggestions for using the system.

Find the most current online test at **www.acrpnet.org/homestudy**, including any revisions made after publication of this issue of *Clinical Researcher*.

15. **What is necessary for system validation?**

A. Vendor-provided documentation that the system is compliant is all that is necessary.

B. Test driving the system once by randomly checking various components to determine that it is usable.

C. Approval by the FDA indicating that the system is acceptable and in compliance with Part 11.

D. Initial and ongoing systematic testing of the system by the site to confirm that it is functioning as intended.

16. **Which of the following statements are true regarding training requirements for Part 11 compliance?**

1. Training should only be performed upon system implementation.

2. Training should be consistent with the function/responsibility of the end-user.

3. The processes surrounding how and when training is conducted and documented is a responsibility of the site.

4. The processes surrounding how and when training is conducted and documented is a responsibility of the vendor or sponsor.

A. 1 and 3 only

B. 1 and 4 only

C. 2 and 3 only

D. 2 and 4 only

17. **When evaluating site standard operating procedures (SOPs), which SOPs are necessary to support the requirements of Part 11?**

1. Vendor selection/audit

2. Records management

3. CRF quality assurance

4. Electronic signature policy

A. 1, 2, and 3 only

B. 1, 2, and 4 only

C. 1, 3, and 4 only

D. 2, 3, and 4 only

18. **What are the key system features of a Part 11–compliant system?**

1. Integration with FDA gateway

2. Records available for export and review throughout the retention period

3. Automatic tracking of changes to electronic records

4. Automatic tracking of name, date, time, and Statement of Testament associated with signature

A. 1, 2, and 3 only

B. 1, 2, and 4 only

C. 1, 3, and 4 only

D. 2, 3, and 4 only

19. **A review of a Part 11–compliant system's features and functions that a site will use is the responsibility of which of the following?**

A. The sponsor

B. The site

C. The vendor

D. A combined effort

20. **When should training on a Part 11–compliant system be performed?**

A. Only upon implementation

B. Only when major system changes occur

C. Upon implementation and annually

D. Upon implementation and with any major changes

Using EHR Data Extraction to Streamline the Clinical Trial Process

21. **Extracting real-time patient data through EHR technology allows a sponsor to ultimately do which of the following?**

1. Accelerate trial timelines

2. Identify cohorts of subjects eligible for a study

3. Qualify investigators

4. Lower costs

A. 1, 2, and 3 only

B. 1, 2, and 4 only

C. 1, 3, and 4 only

D. 2, 3, and 4 only

22. **What will the universal adoption of EHR technology require?**

A. Enhanced protected health information (PHI) data security

B. A combination of public and private grants and funding

C. Patient consent

D. Larger datasets from multiple healthcare organizations

23. **What has the Case Comprehensive Cancer Center done with its automated EHR tool?**

A. Recruit patients for upcoming clinical trials

B. Allow physicians to match their patients with active clinical trials

C. Assist investigators with protocol design

D. Match physicians to patients

24. **What aspect of EHR technology greatly improves the recruitment stage of a clinical study?**

A. Re-identification of a patient only after a healthcare organization has agreed to participate in a trial

B. Re-identification of a patient before a healthcare organization has agreed to participate in a trial

C. Re-identification of a patient during research

D. Re-identification of a patient at any time

25. **Which of the following are current drawbacks to utilizing EHR technology?**

1. Missing data

2. PHI protection and security

3. Lack of policies regarding secondary use of the data

4. No affordable access options for small pharmaceutical firms/contract research organizations

A. 1, 2, and 3 only

B. 1, 2, and 4 only

C. 1, 3, and 4 only

D. 2, 3, and 4 only

26. **"Mapping clinical data" refers to what?**

A. Tracing disparate clinical data back to each patient's electronic medical record

B. Applying searchable codes to a dataset

C. Conducting an extensive manual review of clinical data and unifying the data to a standard terminology

D. Ongoing data maintenance by institutional review board experts

27. **What was ICON able to achieve by leveraging EHR data?**

A. Provide real-world data to support a broader range for HbA1c lab eligibility criteria

B. Identify an alternative lab to replace HbA1c

C. Construct data-driven recommendation to not change the minimum value for a lab eligibility criteria

D. Find 30 additional patients to recruit into the study

28. **What was the retrospective analysis using EHR data assessments able to prove?**

A. Some amendments could have been avoided by upfront protocol feasibility testing.

B. Cohort size comparisons were not always useful.

C. EHR analytics provided to a key opinion leader were highly influential in the leader's decision making.

D. Cohort identification technology identified 23 potential subjects to enroll.

29. **EHR data have been validated for representativeness and reproducibility of what?**

A. Insurance claims

B. Socioeconomic status

C. Epidemiologic findings

D. Risk-based monitoring needs

30. **Which of the following are future benefits of leveraging EHR data?**

1. Improved clinical outcomes

2. Getting new therapies to market faster

3. Cost savings

4. Investigator motivation

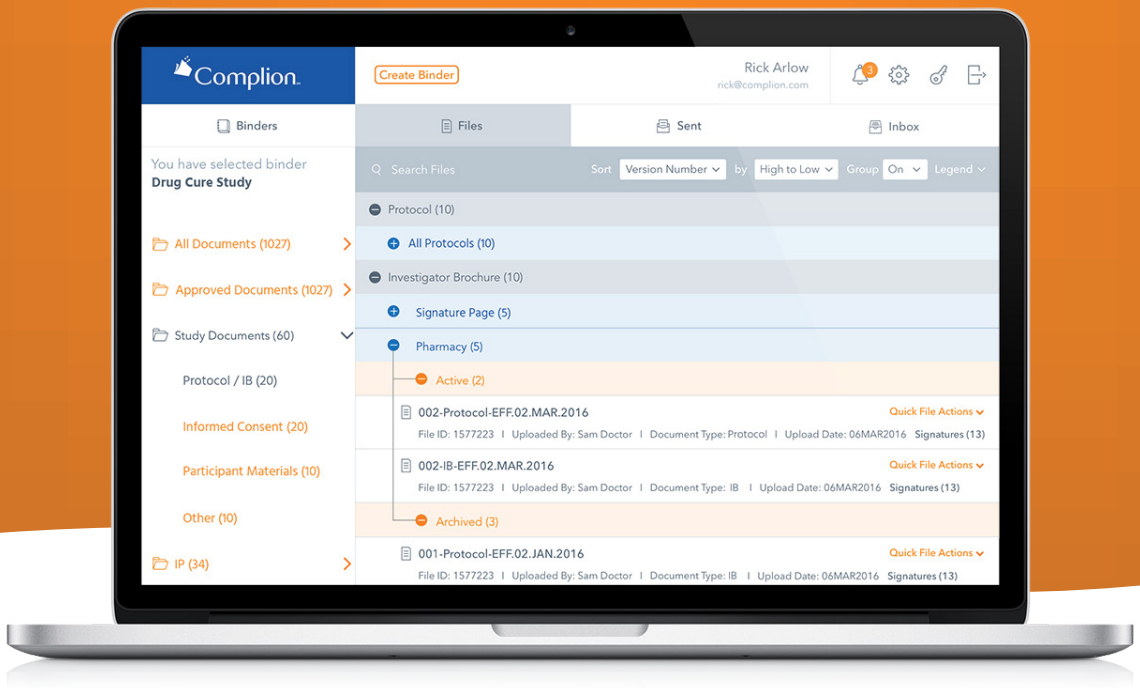
A. 1, 2, and 3 only

B. 1, 2, and 4 only

C. 1, 3, and 4 only

D. 2, 3, and 4 only

GO PAPERLESS. STAY COMPLIANT.



Are you tired of fighting with messy binders, cluttered inboxes or misplaced documents? Is the accumulation of regulatory and administrative tasks adding to your already heavy workload?

Complion helps clinical research sites save time and focus on your trials by reducing the hassle associated with managing regulatory and trial paperwork.

- Find the right document quickly with beautifully organized files, standard templates, and powerful keyword searching
- Save time managing PI delegation records, Safety Reports, CVs, Licenses and training with Part 11 compliant signatures and workflows built for you
- Eliminate printing and redundancy by connecting to your existing email, CTMS, IRB or EMR systems without costly development or custom coding
- Collaborate across multiple sites and institutions instantly
- Partner with our team of certified clinical professionals to learn best practices, train your team, and maintain 21 CFR Part 11 compliance

Complion℠

Complion is a proud ACRP Alliance Partner

Join the leading sites, hospitals, academic medical centers and cancer centers around the country using Complion to streamline paperwork and improve compliance.

UR Medicine Wilmot Cancer Institute — Medicine of the Highest Order
CRC Group
Mary Crowley Cancer Research — Hope Lives Here
optimed Research, LTD
ACR Advanced Clinical Research
Del Sol Research Management, LLC

Contact us today!

800-615-9077
www.complion.com
sales@complion.com

How *Tech Integrations* are Changing Clinical Research

GOOD MANAGEMENT PRACTICE

Jim Primerano

[DOI: 10.14524/CR-17-4010]

In the first integration of its kind, the merger of electronic clinical outcomes assessment (eCOA) and randomization and trial supply management (RTSM) technologies is revolutionizing clinical trials. The unique and obvious combination provides sites, sponsors, and patients with a single source of hardware to support trial logistics and supply chain management, ensuring that trials are interconnected and orderly, not disruptive.

Though relatively new to the field of clinical research, the merger of eCOA and RTSM technologies is making its advantages known. By mitigating the need for separate vendors, which burdens the sponsors who largely are responsible for coordinating the value of data, the integration offers users a single implementation model and, ultimately, a streamlined umbrella for data collection and activities.

From advanced compliance analysis and operational controls to cost savings and higher data quality, the integration is poised to prosper—especially as additional case studies and quantitative key performance indicators emerge.

The Impending Road to Adoption

Pharmaceutical sponsors are beginning to consider how integrating these tools can add more value. One challenge to adoption is that many studies still rely on paper for patient-reported and clinician-reported outcomes in trials, but the migration to eCOA is steady and clinicians generally prefer electronic tools when implemented effectively.

The evidence in support of eCOA is compelling in terms of better data quality, fewer missing data points, and more encouragement by regulators. RTSM is already a well-established and accepted technology, and the increasing use of eCOA is an important catalyst for bringing the two technologies together.

On its own, eCOA is another distinct system, but when joined with RTSM it produces a richer data set that is centralized on quality outcomes data and baseline metrics.

Advantages of eCOA and RTSM Integration

Undeniably, interoperability is a staple—it's the crucial functionality that allows operational data to be leveraged across disparate systems. On its own, eCOA is another distinct system, but when joined with RTSM it produces a richer data set that is centralized on quality outcomes data and baseline metrics. In addition to offering a complete end-to-end solution, the integration boasts myriad advantages:

Advanced Compliance Analysis

The integration leverages data from RTSM with data recording in eCOA to produce a richer data set. By aggregating the disparate sources of data into a comprehensive view, sites and sponsors can obtain greater analytics at the patient and site levels and assess compliance of the outcome itself.

Clinical Operation Components

On a small scale, operational controls can be enabled through the integration. The aggregation and analysis of data can help determine patient eligibility for clinical trials at the randomization point, and can ensure that only qualified patients are enrolled. Maintaining control of eligibility criteria allows sponsors to streamline processes, mitigate errors, and gain greater control around discontinuation and patient status.

Sponsor Cost Savings

From a service cost perspective, the integration of eCOA and RTSM provides ample efficiency gains in project management. From a technology stack perspective, both eCOA and RTSM are built on the same framework; by leveraging this, sponsors can more easily achieve interoperability. Rather than amassing charges for separate vendors, contracts, and engagements, the integration brings all of the components under one umbrella, including the final coordination and identification of the data value itself.

Analyzing the Best Use Cases

Designed with a better user experience in mind, the integration of eCOA and RTSM has been thoughtfully developed with site and patient requirements at the forefront. As a result, the technologies incorporate functionalities required across all clinical research studies, such as enhanced flexibility, patient perspective, and "bring your own device" features, among others.

The integrated technology has been particularly successful for use in diseases with complicated patient screening procedures and inclusion and exclusion criteria. For example, in studies with Alzheimer's patients, leveraging the integrated intelligence can drive greater statistical validity, reduce site burden, and improve the overall data quality.

Other highly qualified use cases include those in which outcome data are the primary endpoint. This is often found in psychiatry-oriented trials and oncology, as data tend to be more subjective. In a clinical trial for oncology, patients are recording data related to quality of life, not just quantitative remission metrics, and the integration successfully fills the gap for data collection centered on subjective pain.

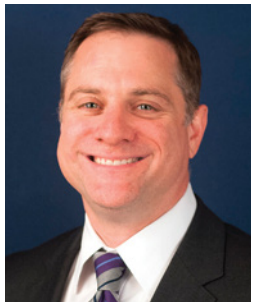
More eCOA and RTSM Trends

Trial technology that focuses on increasing patient engagement and compliance can lead to better outcomes. While the integration of eCOA and RTSM provide a good user experience, the technology's thoughtful, individual features are the driving force behind patient engagement.

For example, SMS text messaging support for patients and stakeholders can expand medication compliance; be leveraged to issue alerts to clinical trial sites, study sponsors, and contract research organizations; and provide effective solutions for adherence to long-term therapies in chronic disease. In fact, there's increasing evidence that text messaging is an effective and scalable tool for improving medication adherence among patients. A study review in the February 2016 issue of *JAMA Internal Medicine* reported a 50% increase in adherence rates when text messaging was utilized; high acceptance and satisfaction levels among most participants; and text messaging support as a valuable reminder with ease of use.

Conclusion

With ample data to further support the impending technology revolution, the integration of eCOA and RTSM is an obvious combination. Reliant on the imminent adoption of eCOA, which will undoubtedly demonstrate its keen ability to reduce data variance, increase patient compliance, and decrease site monitoring costs, the acceptance of eCOA and RTSM integration is just around the corner. Its universal adoption will be the calm after the storm.



Jim Primerano (jim.primerano@bracketglobal.com) is senior vice president and general manager for the eClinical division of Bracket, a company focusing on clinical research data services and technology based in Wayne, Pa.

Randi Foraker, PhD, MA, FAHA

[DOI: 10.14524/CR-17-4008]

Conducting Research with EMR Data? You Need an Epidemiologist

Researchers have long characterized the etiology of disease using data from population-based cohort studies, such as the Framingham Heart Study.[1] Cohort studies such as these comprise decades of follow-up and rich amounts of questionnaire and physical exam data; however, they are also expensive endeavors. Electronic medical record (EMR) data represent a resource-efficient source of information for researchers to use as they investigate myriad disease states, and these data are particularly pragmatic for answering health services–related research questions.

As EMR data grow in popularity as a secondary data source for researchers, it is critical to establish best practices for data generation, study design, and data analysis.

Due to the convenience of these data, which are collected electronically at medical centers and clinics across the United States,[2] their use for research purposes is becoming ever more common.[3] Still, using secondary data comes with inherent pitfalls stemming from the fact that the data were either not originally collected for research purposes, or were not collected to answer a particular research question. Further, data central to a research question may be missing from the dataset or characterized in a way that is not ideal for the analysis.[4]

As EMR data grow in popularity as a secondary data source for researchers, it is critical to establish best practices for data generation, study design, and data analysis. As experts in study design, epidemiologists have the necessary skills and tools to anticipate the effects of, and in some cases account for, threats to internal validity (e.g., confounding, selection bias, information bias), and to deal with the implications of the concept of representativeness for the ability of the study's results to translate to the population level to improve health.

The rest of this column addresses internal validity and representativeness, and suggests some related solutions and strategies for implementation across data platforms.

Internal Validity

Confounders are factors that explain, completely or in part, the effect of a given exposure on an outcome.[4] In any dataset, confounders may be measured or unmeasured. Adequate control for confounding is a concern when using EMR data, since many confounders (i.e., comorbidities) go un- or under-documented. For example, one limitation of using EMR data for research purposes is that one often cannot adequately characterize the social and behavioral determinants of health from the available data.

Meanwhile, selection bias results from factors differentiating study participants from all those eligible to participate.[4] For example, when a research sample is drawn from a population of inpatients, it must be acknowledged that the findings that arise from that sample are going to represent the experience of patients who are generally sicker (i.e., in terms of disease stage or severity of illness) than others. Selection bias can also arise when choosing controls from a hospitalized patient population for a case-control study, as there exists a risk of selecting controls who are not representative of the source population (i.e., all patients without

FIGURE 1: STRENGTHS, OPPORTUNITIES, AND LIMITATIONS OF USING EMR DATA FOR RESEARCH

Convenience
Detailed diagnoses and health services data

Merge with other data sources
Apply epidemiologic principles

Lack of data on confounders
Selection factors misclassification

the disease of interest) in terms of exposure prevalence. Choosing a sample of controls from a hospitalized patient cohort, for example, may yield a different exposure-outcome association that would have been observed had a random sample of the source population been selected instead.

Another internal validity concern—information bias—can arise from differential or nondifferential misclassification. In epidemiological studies, misclassification of the exposure, outcome, or confounders can occur.[4] Nondifferential misclassification of a study outcome happens when the extent of misclassification changes according to level of exposure or the value of other confounding variables. An example in the clinic setting would be if the determination of the outcome for all patients is made by a laboratory test done with uncalibrated equipment.

Often of greater concern are the results of differential misclassification leading to an over- or under-estimation of an effect. In EMR data, an exposure such as smoking status may be more accurately defined and up-to-date for patients with lung cancer compared to patients without lung cancer. In this simple example, if current smoking is under-recorded in patients without lung cancer and accurately recorded among patients with lung cancer, then the observed relationship of smoking to lung cancer would be exaggerated in the dataset.

Representativeness

Patients seen at a single clinic or medical center within the population's catchment area may not represent the "typical" patient from the target population. That means that, even if the internal validity of the study is high, the observed associations may not apply beyond that sample of patients. Of note, internal validity should be prioritized above generalizability of the results, since lack of internal validity precludes external validity.

Proposed Solutions

Several strategies can be applied to enhance the internal validity of EMR data for answering our most important clinical research questions. Some of the solutions proposed below involve capitalizing on other sources of data, and others require more careful treatment of the EMR data at our fingertips (see Figure 1 for an overview of the strengths, opportunities, and limitations of such data). These solutions are:

- Data on unmeasured confounders may be obtained by linking EMR data to other sources, such as socioeconomic data from the U.S. Census or patient-reported outcomes and behavioral data from questionnaires. If researchers suspect that data on a particular confounder are under-documented within a single field in the EMR, they may choose to develop an algorithm incorporating multiple sources of data from the EMR.
- Results should always be interpreted consistent with how the data were collected. Investigators should also carefully consider from which population a comparison group will be selected; in many cases, publicly available data may be used to characterize controls selected from the general population.[4]
- To combat information bias, data should be generated and stored in the same way, regardless of the exposure or disease status of the participant. Researchers using EMR data often do not have control of the manner in which the data are originally collected, and should be prepared to link EMR data with other sources (i.e., patient-reported outcome questionnaires) and to conduct sensitivity analyses to assess the robustness of the findings to potential misclassification.

A challenge to be faced when conducting observational studies in the EMR is that one doesn't, and won't, know the "true" association between a given exposure and a disease.

- Representativeness of data can be assessed by comparing the distribution of key demographics in the clinical sample to that of the target population. For a given clinic or medical center, the catchment area can be thought of as the target population. Quantifying these differences, if they exist, should be considered the first step. If few differences exist, stronger inferences can be made. Otherwise, once the researcher knows how much the study population differs from the target population, the second step should employ the observed differences to weigh or standardize the observations in the analytic dataset.[5]

Conclusion

A goal of investigators should be to accurately estimate the association between a given exposure and disease, or in some cases to build a predictive model to account for all sources of variability in the study outcome. A challenge to be faced when conducting observational studies in the EMR is that one doesn't, and won't, know the "true" association between a given exposure and a disease.

The researcher's job is to use the tools at his or her disposal to approximate the truth as closely as possible. Enhancing the internal validity of studies using EMR data may require them to leverage additional sources of data, minimize the influence of selection factors, and conduct sensitivity analyses. Steps can be taken in the study design phase to ultimately enhance both internal and external validity. They should also consider consulting a local epidemiologist for specific guidance regarding the research project at hand.

Randi Foraker, PhD, MA, FAHA, (rforaker@cph.osu.edu) is associate professor of epidemiology and biomedical informatics at The Ohio State University College of Public Health.

References

1. Dawber TR, Meadors GF, Moore FE. 1951. Epidemiological approaches to heart disease: the Framingham Study. *Am J Pub Health Nation's Health* 41(3):279–86.
2. HIMSS Analytics. Healthcare Information and Management Systems Society. Electronic Medical Record Adoption Model. www.himssanalytics.org/healthcare-provider-models/all
3. Kite B, Tangasi W, Kelley M, Bower J, Foraker R. 2014. Electronic medical records and their use in health promotion and population research of cardiovascular disease. *Curr Cardiovasc Risk Rep* 9(1):1–8.
4. Rothman KJ, Greenland S, Lash TL. 2008. *Modern Epidemiology* (3rd ed). Philadelphia, Pa.: Lippincott Williams & Wilkins.
5. Bower JK, Bollinger CE, Foraker RE, Hood DB, Shoben AB, Lai AM. 2017 (in press). Active use of electronic health records and personal health records for epidemiologic research. *eGEMs*.

ACRP 2017 MEETING & EXPO

SEATTLE, WASHINGTON — APRIL 28 – MAY 2

Innovation. Implementation. Collaboration.

See the future of clinical research at the ACRP Meeting & Expo. Learn from the influencers, innovators, and regulators driving change in clinical trial operations. You and your team will gain practical strategies to manage change, streamline operations, and minimize risk. Position yourself for success at the premier education and networking event for clinical research professionals.

Who's Attending?

2,000+ Clinical Research Professionals, Including Trial Coordinators, Monitors, Investigators, Project and Site Managers, Patient Recruiters, and More

100+ Expert Speakers from Sponsors, CROs, Sites, Regulatory Agencies, and More

100+ Exhibiting Companies and Organizations

Why Should You?

100+ Educational Sessions Uniquely Tailored to Professionals Conducting Clinical Trials

Networking Opportunities for Peer-to-Peer Exchange and Engagement

Ability to Earn Continuing Education Units

On-Demand Access to All ACRP 2017 Sessions through the Online Conference Library for 2 Years

What's New for ACRP 2017?

- More Advanced-Level Content for Experienced Professionals
- Educational Sessions for a Broader Spectrum of Professionals
- Greater Emphasis on Practical Application to Improve Trial Operations
- "Master Series" Helping Put Theories into Practice
- Educational Content Aligned with Core Competencies for Clinical Research Professionals

Program Highlights*

FRIDAY, APRIL 28 - PRECONFERENCE WORKSHOPS

Hands Across the Water: A Comparison of Clinical Trials in the EU and U.S.
Practicing Good Science Through Ethical Study Design
GCP Auditing: Apply Your New Skills at Work
Tools to Help Clinical Sites Optimize Performance and Maintain GCP Compliance
Fine-Tune Your Vulnerability Radar: Protecting the Vulnerable
Unlocking the Value of Ethics Using Educational Games

SATURDAY, APRIL 29

Mastering Your Response to the Dreaded FDA Form 483
Wearables and Big Data: The New Gold Standard for Clinical Trials
The Seismic Shift in the Monitoring Paradigm: From Quality Control to Quality Assurance
eConsent: Preparing for Paperless Consent
Going Paperless: A Smart Way to Increase Site Efficiency and Save Resources
The 2016 Medical Device Directive: What It Means to You

SUNDAY, APRIL 30

Investigator Attrition: Strategies to the Turn the Tide
The ICH GCP E6 R2 Revisions: Impact on the PI and Site
Bring Your Own Device: Is it Right for Your Clinical Research Enterprise?
Forging a New Path to Professionalism: GCP vs. Core Competency-Based Training
Maximizing the ROI of Your Clinical Trial Management System
Melding Consumer Big Data with Medical Big Data: The Regulatory and Ethical Implications

MONDAY, MAY 1

Beyond Audit Survival: The Busy Professional's Guide to Audit Preparation
Trends, Strategies, and Tools for Achieving Informed Consent
Build a Better Site Budget to Ensure Trial Success
Putting Patient-Centric Principles into Practice
2017 Update: U.S. Healthcare Regulatory Changes and their Impact on Clinical Research

TUESDAY, MAY 2

Medical Cannabis: A Substitute for Prescription Opioid Use?
The Power and Reach of Social Media in Clinical Trials
Optimize Workflow and Resource Allocation Using LEAN-R
Returning Research Test Results: Know Your Ethical and Legal Obligations

* Subject to Change

HOTEL & TRAVEL

Book your room through ACRP to make sure you get the lowest guaranteed rates on your stay in Seattle. Plus, you can save 10% on your flight by flying Delta.

ATTENDEE ROI TOOLKIT

Use the attendee ROI toolkit to gain employer support for your trip to ACRP 2017. Show the return on investment you and your organization will enjoy.

GROUP DISCOUNTS

Save $100 on your registration with special discounts for groups of three or more colleagues from the same organization.

CONFERENCE.ACRPNET.ORG

Visit us online to register or learn more about the ACRP 2017 Meeting & Expo.

ACRP
FOR LEARNING FOR LISTENING FOR LIFE

[DOI: 10.14524/CR-17-4009]

Sandra "SAM" Sather, MS, BSN, CCRA, CCRC; Mika Lindroos

Breaking Down the Barriers to eConsent Adoption

Obtaining informed consent from patients is fundamental to the successful conduct of all clinical trials. It is critical that every patient understands the requirements and expectations of participating in a protocol, so that he or she can make an informed and voluntary decision to take part. Too often, however, informed consent is mistakenly viewed as synonymous with obtaining a handwritten signature on a paper consent form.

To help improve the process of obtaining consent from research participants, the industry is seeing increased interest in automated electronic informed consent (eConsent) approaches.

On the contrary, the main priority of the informed consent process should be to provide patients with adequate information to support their decisions, facilitating and confirming understanding of that information, and providing an appropriate amount of time for patients to ask questions and air any uncertainties about their involvement. The consent process should also focus on continuing to provide up-to-date information to patients as a clinical investigation progresses.

To help improve the process of obtaining consent from research participants, the industry is seeing increased interest in automated electronic informed consent (eConsent) approaches. However, some sponsors and investigators are understandably wary of integrating another technology platform into their clinical trials. Some of the perceived barriers include concerns regarding cost, privacy, and compliance. The industry still has work to do in making a case for eConsent to be adopted as a best practice.

The Evolution of Consent

It has been obvious for a while that current informed consent processes and oversight need improvement. As with many other processes in clinical research, informed consent has traditionally been obtained via lengthy, paper-based methods. Researchers tend to view consent as a means to present participants with extensive legal information relating to a clinical trial, rather than seeing it as an opportunity to provide concise and readily accessible study information.

Informed consent is not just a regulatory document, but is a teaching tool as well. It should not only serve the participant at the beginning of the study, but should be a support tool throughout the duration of a study.

The current approach to consent management has challenges in areas such as these:

- Inefficient and ineffective consent development and version management
- Poor consent process documentation sometimes linking to data loss
- Lack of participant understanding contributing to lack of subject compliance to the study requirements and low subject retention levels
- Increased costs across the study lifecycle for monitoring and issues management
- Oversight of the consenting process by investigators, sponsors, and institutional review boards (IRBs) when using paper-based processes

The above challenges are troublesome without even considering the additional complexities brought by today's multicentered trials and the multiple consent forms which exist for each study.

At its core, eConsent provides an accurate, efficient, and cost-effective method to solicit and track questions about a subject's participation in a clinical trial and document that those questions have been answered.

In a time when data acquisition and capture in clinical research are increasingly managed via electronic solutions, it is a logical step to do the same for obtaining informed consent. To combat the inefficiencies associated with outdated paper processes, eConsent better utilizes learning principles in communicating study information to patients, representing a major advancement in improving patient comprehension in clinical research.

eConsent uses electronic systems and multimedia, including audio, graphic, and video features, to securely obtain and document informed consent. Through the use of digital timestamps, consistent version control, real-time remote monitoring, and ongoing tracking, eConsent solutions can provide a clear audit trail for every participant in every clinical trial.

FDA Backing

The U.S. Food and Drug Administration (FDA) has recently released its final guidance document surrounding the use of eConsent in clinical trials. The guidance supports companies that want to take an electronic approach by clarifying how regulators will permit companies to use electronic means to fulfill the Office for Human Research Protections and FDA requirements for informed consent and IRB review.[1]

While this guidance is applicable to studies that are conducted within the United States, it may also serve as a suitable reference document as sponsors, investigators, and ethic committees around the world consider how they will work with eConsent. The guidance provides recommendations on ways to implement eConsent to help:

- Ensure the protection of the rights safety and welfare of participants
- Facilitate the participant's comprehension of the information presented during the eConsent process
- Ensure the appropriate documentation of consent obtained when electronic systems and processes are used to collect informed consent
- Ensure the quality and integrity of eConsent data included in FDA applications and made available to FDA during inspections[1]

The Benefits of eConsent

At its core, eConsent provides an accurate, efficient, and cost-effective method to solicit and track questions about a subject's participation in a clinical trial and document that those questions have been answered. eConsent can support participants' comprehension and retention of study details through tiered information delivery, with essential information presented in the main body of the consent and more detailed information placed in a separate section.

Further, eConsent systems can be set up to ensure only authorized site personnel obtain consent. Real-time reporting of data and feedback mechanisms may also reveal key information, such as words or concepts, which participants have difficulty comprehending.

While sponsors have previously had to rely on manual processes to report on consenting, electronic systems include trial management features to support oversight. eConsent can remotely track consenting and reconsenting rates across large, multisite studies; the derived metrics can provide an immediate picture of what is happening in the realm of consent across a study at any given time.

eConsent can also mitigate regulatory risk of data loss due to inadequate consent by enforcing the completion of certain activities prior to a patient being able to achieve a "consented" status. Further, the use of eConsent may help to facilitate more timely updates to participants about new information pertaining to a trial, accelerate the enrollment process, and allow subjects to consent no matter where they are located.

Informed consent is not just a regulatory document, but is a teaching tool as well. It should not only serve the participant at the beginning of the study, but should be a support tool throughout the duration of a study.

Barriers to eConsent

Many of the barriers currently slowing the adoption of eConsent are related to some of the myths surrounding the implications of its use. In integrating an electronic approach to informed consent within a clinical trial, one of the major hurdles for sponsors is the reluctance to replace existing paper-based consent processes with a new electronic system and supporting processes. Taking the time to develop work streams that integrate eConsent is an important step to ensure the integration is not creating more burdens for study teams, sites, and IRBs.

It is likely that many sponsors would prefer to integrate eConsent with other current electronic platforms, such as trial management or electronic clinical outcome assessment (eCOA) solutions. Additionally, research institutions with electronic health records (EHRs) may wish for the signed consents and associated data to be easily uploaded to the participant's EHR.

To ensure a smooth transition and improve clinical trial operations and oversight, sponsors, IRBs, ethics committees, and research sites should evaluate which systems offer the most benefits for

integration. It is also important for sponsors to understand that, when identifying how to integrate eConsent into a protocol, the tool itself should not lead to a longer development time for the consent. Streamlining and integration will again be important factors here in making the whole process as efficient as possible.

Final Thought

Modern clinical trials are complex, and it is easy to see why so many research participants struggle to both obtain and understand information relating to their participation. This low level of engagement leads to reduced quality outcomes, including missing or incorrect data and poor retention levels.

In a bid to overcome the widespread challenges, there is little doubt that the future of obtaining informed consent in clinical trials will increasingly lie with electronic methods. Although sponsors my encounter hurdles surrounding how to integrate eConsent systems into study designs in the short term, working to identify practical means to introduce these solutions into their protocols will undoubtedly contribute significant rewards in the long term.

Reference

1. U.S. Department of Health and Human Services. 2016. Use of Electronic Informed Consent—Questions and Answers: Guidance for Institutional Review Boards, Investigators, and Sponsors. https://www.fda.gov/downloads/drugs/guidancecompliance regulatoryinformation/guidances/ucm436811.pdf

Sandra "SAM" Sather, MS, BSN, CCRA, CCRC, (sam.sather@crfhealth.com) is the quality and regulatory lead for CRF Health's TrialConsent and cofounder of Clinical Pathways, LLC. She also is a member of ACRP's Academy Board of Trustees and Regulatory Affairs Committee, and has been dual certified through ACRP for 15 years.

Mika Lindroos, (mika.lindroos@crfhealth.com) is director of product management at CRF Health, and has more than two decades of experience in software product management in the global environment.

A CASE STUDY IN

Redefining Regulatory Binder Management

PEER REVIEWED | Hether Seifert, MSM, CCRP | Becky Bosch

[DOI: 10.14524/CR-16-0026]

Paperless regulatory document management is a hot topic today among personnel at study sites, contract research organizations (CROs), and sponsors facing what is often overwhelming paperwork that seems to grows exponentially with each new trial. Many institutions are starting to invest in regulatory document management solutions to increase staff productivity, speed study start-up, and improve inspection readiness.

However, simply going "paperless" does not solve the core document management issues of workflow, change, and signature management, especially in a complex environment. Understanding how others have identified and addressed these issues can help an organization examine its own operations.

FRAMING THE PROBLEM

Clinical trials require regulatory documents to capture the activities performed before, during, and after the accrual of participants. These documents may vary depending upon the type of trial and regulatory requirements, but typically contain the study protocol, institutional review board (IRB) approvals, informed consent forms completed by participants, copies of *curricula vitae* and medical licenses of study investigators, financial disclosures, package inserts (in device studies), the Form FDA 1572 ("Statement of Investigator" required by the U.S. Food and Drug Administration in drug studies) or Investigator Agreements (required by FDA in device studies), the site's delegation of authority log, and many more. This collection of essential documents is referred to as the regulatory binder.

When an individual at a site is responsible for one regulatory binder, and all staff are based at the same location, document management is not complex. However, when the person managing the binder is not located at the same location as the investigators and the files need to be shared across locations, the problem starts to make itself evident.

A popular solution at this point is to move to a paperless or electronic shared server environment, in which documents are scanned and uploaded to a shared server space for easy electronic access, and then manually tracked via spreadsheets. The person responsible for the electronic binder ensures that document updates, for example staffing changes, are scanned and uploaded to the server. This procedure via a shared server with manual document management can meet the needs of small to midsized research organizations.

However, as the number of trials conducted simultaneously at a site increases, the existing individual or team managing regulatory binders may no longer be able to handle the mounting workload. Document management becomes much more complex due to the volume of trials, locations, staff, and updates, as well as the complexities of document coordination across supporting staff. Lost documents, missing document updates, and spreadsheet discrepancies are inevitable within even the most tightly run organizations. It now becomes clear that a manual or hybrid process of document management does not support the fast-paced study environment of a large research operation.

CASE STUDY: FACING CONFUSION, SEEKING CLARITY

Let's consider the case of a research center that used to have just one person managing trial documentation by keeping paper copies in binders that were shipped to monitors at different physical locations for each visit. It was time consuming for the staff member to manage such clunky binders, and for the monitors to manually go through the paper documents to determine what had already been reviewed and what was new.

With more than **650** trials, the staff was supporting more than **100,000** documents.

As the research center grew, the number of trials and supporting staff increased. Sharing and managing paper documents across an increasing number of staff and physical locations was challenging. It had become evident that regulatory binders could no longer be maintained efficiently in the paper format, so the decision was made to move to an electronic format on shared server space. It was assumed that this tactic would deliver improvements in study efficiency and reduce staff workload by simplifying document sharing, storing, and updating.

Under the new process, documents were routed for physical signature via e-mail, scanned, and uploaded into a standard set of folders using an agreed-upon naming convention, in an attempt at standardizing the tasks. Trial statuses were tracked by each staff member using personal spreadsheets. When monitor visits were scheduled, rather than sending a physical binder of documents, a disk with copies of all relevant documentation from the shared server was created; monitors then spent time deciphering the organization of files on the disk and reviewing all documents to find new and updated information.

This hybrid electronic solution with manual tracking, while an improvement over the former, completely paper-based process, did not deliver the anticipated workload efficiency benefits. It did not solve, but exposed, what proved to be the root issues driving staff workload—document change management, tracking, retention, and preparing for monitor visits.

The research center continued to grow—as did the number of trials—to the point that additional staff were required to support the volume of activity and cross-coverage of duties. Each basic regulatory binder had a minimum of 179 documents [(2 labs per trial x 2 documents per lab) + (50 staff per trial x 3 documents per staff) + (25 study docs)]. With more than 650 trials, the staff was supporting more than 100,000 documents.

At this point, the document management task was overwhelming. The electronic shared server solution was not adequate; however, it did uncover the root issues that needed to be addressed.

THE SEARCH FOR A SOLUTION

Simplifying the management and sharing of thousands of regulatory documents across multiple trials, locations, and staff would require an automated solution that addressed the core issues driving staff workload—document change management, tracking, retention, and preparing for monitor visits. The new solution needed to:

- Enable staff to submit a document update once, then automatically update all trials using that document
- Streamline the visibility of trial and document statuses
- Electronically capture 21 CFR Part 11–compliant signatures in adherence to the *Code of Federal Regulations*
- Replace paper documents with online documents that met regulatory retention requirements
- Securely share trial documents online anywhere, anytime, from any device

As with any large problem, the standard barriers existed in terms of funding, staffing and expertise, viable solutions, implementation time, and availability of internal information technology (IT) resources.

The search began with "off the shelf" solutions. The evaluation found challenges with packaged solutions in that, first, the cost of such solutions evaluated were prohibitive; second, in terms of the need to adapt business processes to the software; and third, regarding the requirement for integration resources from the internal IT team. These challenges added to the overall expense with the hidden costs of adaptation and process updates, internal IT costs, and implementation delays based on the internal IT queue.

The next option explored was a "home built" system developed by internal IT staff. The evaluation found this could be more expensive, and would still require business processes changes to adapt to the developed solution. The traditional software development process would require significant time from the trial staff and internal IT staff. With the large IT workload queue, a solution was anticipated to be years away.

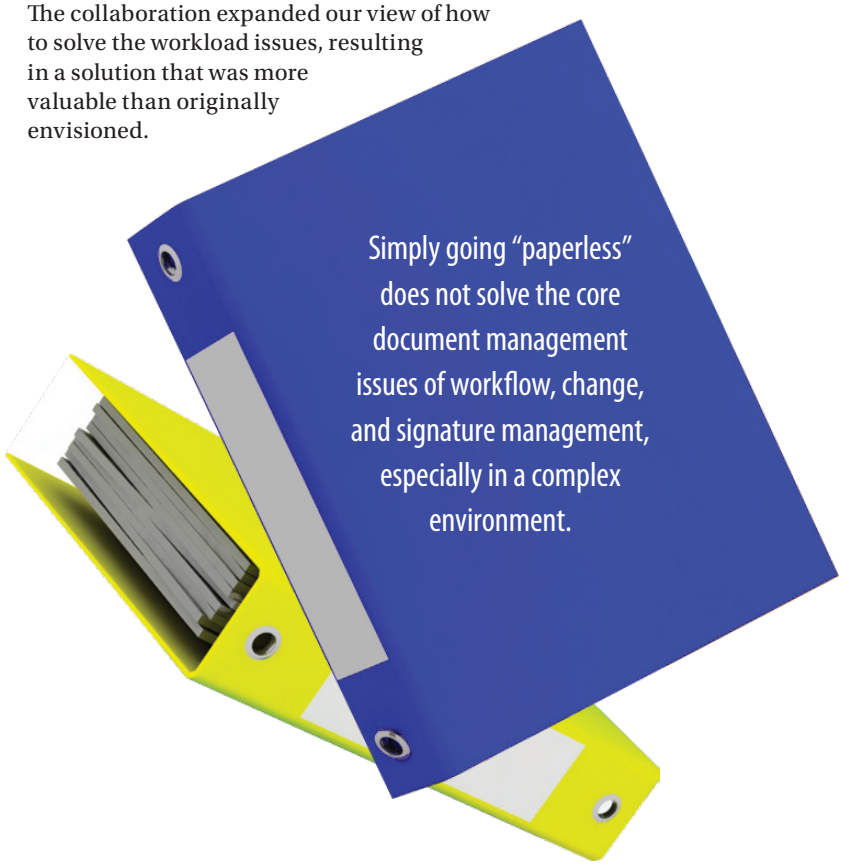
The third option was to collaborate with a custom software expert to develop a custom solution. This was the least expensive and quickest strategy to implement. Utilizing an iterative and incremental development methodology, less time was required from trial staff to define and develop the solution. The resulting solution was developed in four months and rolled out in phases, to allow the staff time to adjust to a fully automated solution. While the system was designed by the users, there was a bit of adjustment required, as old manual processes were no longer needed, and staff gained capacity to do more.

The final solution delivered the advantages of centralized document management via a single master source of documents, eliminating duplicate documents with mismatched updates. When document updates are entered, such as a CV with new details, the change is submitted once and all related documents and trials automatically and instantly have the updated information.

The solution is a cloud-based approach with anywhere, anytime, any device access. It incorporates e-signatures and e-forms, allowing investigators to sign documents from anywhere in the world using their tablets or phones. Monitors now log in remotely to access up-to-the-minute documents, and can easily identify and review new or changed documents. Regulatory document retention requirements are satisfied and paper binders have been eliminated.

A key lesson from this experience was the importance of selecting the right software development partner. With trial management expertise and no IT background, we benefited from a partner with comprehensive technology expertise that could understand our objectives, help us dig deep into the details to ensure all of the automation opportunities were being considered, and present multiple options with cutting-edge technology. The collaboration expanded our view of how to solve the workload issues, resulting in a solution that was more valuable than originally envisioned.

A popular solution is to move to a paperless or electronic shared server environment, in which documents are scanned and uploaded to a shared server space for easy electronic access, and then manually tracked via spreadsheets.



CONCLUSION

Redefining regulatory document management can deliver new levels of efficiency by focusing on core process improvements in terms of automating and simplifying change management, tracking, document retention, and preparing for monitor visits.

For the research center in this case study, the move to an automated document management process took four months (design, development, implementation) and demonstrated quantifiable results:

- All told, 200 regulatory binders are now managed by each full-time employee (FTE). In addition, each FTE provides cross-coverage for five peers. Significant efficiency increases were achieved by implementing a single master source of documents with updates applied once then available across all trials, as well as the capability of electronic signature capture and secure document sharing.
- There has been a 92% reduction (from an average of 50 hours to just four hours) in the amount of trial start-up time devoted to regulatory document management.

No more waiting on documents in transit, lost on desks, or waiting for investigators to return from travel.

- The time that monitors spend on each trial visit was reduced from an average of 90 minutes to 10 minutes.

Members of the regulatory document management staff have experienced tremendous workload reduction. Principal investigators like the ease of managing and completing online approvals versus paper documents and e-mails. Monitors have responded with comments like "best system yet!" and "I wish everyone had this system. It sure would make life easier!" The system allows all of these trial stakeholders to stay organized and know what documents need review. Even sponsors have responded positively to the system by accepting electronic versions of paper document requests.

Whether an organization manages a dozen or many hundreds of trials, automating binder management can improve efficiency, study start-up times, and inspection readiness. It is hoped that this article helps organizations identify their core issues and potential benefits of an automated solution.

Hether Seifert, MSM, CCRP, (seifert.hether@mayo.edu) is a program manager with the Protocol Development Unit at Mayo Clinic Cancer Center in Rochester, Minn.

Becky Bosch (bbosch@vacava.com) is a client engagement manager with VACAVA Inc.

[DOI: 10.14524/CR-17-4013]

Those Who are Shaping the Shape of Things to Come

Terri Hinkley, RN, BScN, MBA, CCRC, FACRP

As I write this column for the April issue of the *Clinical Researcher,* we are in the midst of finalizing the core competencies for clinical research associates (CRAs), who are also known as clinical study monitors. By the time you read this column, we will have released the final competencies following a 30-day public commenting period.

The process of developing the competencies was extremely challenging but rewarding. The passion and commitment from the industry and those who participated was inspiring. In this column, I would like to acknowledge and recognize the contribution of the volunteers and organizations participating in this groundbreaking work.

LEADING THE CHARGE FOR INNOVATION

The task force of volunteers, 12 of your peers from across a range of organizations in the clinical research arena (see Table 1), worked very hard to critically consider and document the competencies required of clinical monitors at the entry, intermediate, senior, and lead levels. They used the Joint Task Force for Clinical Trial Competence framework as the foundation, and considered a number of competency models available publicly or from their own institutions/organizations in their work. Further, they considered not only the structure of the current monitoring role, but also how the role is evolving and what competencies are going to be required of monitors in the future, and wherever possible they included those competencies in their deliberations.

The steering committee, comprising 11 senior and executive level individuals from several sponsors and contract research organizations (see Table 2), provided the critical oversight and strategic insights needed to ensure we were building competencies that they believe will be the foundation for how monitors are hired, trained, and assessed. They all recognize the need to build the pipeline of CRAs and strongly support the competency model as a means by which new CRAs can enter the role.

LOOKING AHEAD…

We can talk for hours about how we got to where we are, with the requirement for CRAs to have two years of monitoring experience to be billable on studies, but I'd rather talk about the future. The ideal scenario is a future in which we focus on competency as a means of determining someone's ability to successfully monitor clinical studies; a future in which professionals know the knowledge, skills, and attitudes required in each role within clinical research; and a future in which competency—not tenure—takes the starring role in assessing the qualifications of all clinical research professionals.

We at ACRP are very grateful to the task force and steering committee participants, and to their organizations, for freely and happily giving their time and expertise to the development of the competencies and for their ongoing support for competency as the gold-standard for assessing qualification and performance. Please join me in thanking them for all their hard work and commitment to the future of the industry.

TABLE 1: CRA Workforce Development Task Force

Lisa Feeney	ExecuPharm
Tammi Masters	INC Research
Suzanne Day	PRA
David Huston	Covance
Deborah Donnelly	ICON
Bonnie Vlahos	Pfizer
Jeff Wiley	Chiltern
Michael Jimmink	InVentiv
Bev Assman	Genentech
Homan Faraji	Amgen
Patty Darragh	Duke Clinical Research Institute
Barbara Pennington	CoAPCR

TABLE 2: CRA Workforce Development Steering Committee Members

Kathy Goin	Trevena
Carol Seider	Biogen
Cheryl Small	Pfizer
Susan Romberg	Chiltern
Tim Neathery	PPD
David DeMaio	Celgene
Doug Schantz	AstraZeneca
Amy Jimmerson	Medtronic
Stephen Nabarro	Cancer Research UK
Mark Travers	Merck
Melissa Mauriber	Advanced Clinical

Terri Hinkley, RN, BScN, MBA, CCRC, FACRP, (thinkley@acrpnet.org) is the ACRP Workforce Innovation Officer, and had earlier served as Deputy Executive Director.

Merck Lauds Benefits of Core Competencies for Clinical Research Professionals

The Association of Clinical Research Professionals (ACRP) and Merck, along with other leading organizations, have been advocating the professionalization of the clinical trial workforce. In February, ACRP released a harmonized Core Competency Framework for clinical research associates (CRAs) that defines the core competencies required of clinical trial monitors/CRAs within the eight core competence domains for clinical research professionals, as defined by the Joint Task Force (JTF) for Clinical Trial Competence.

The harmonized CRA Core Competency Framework is the product of a cross-industry, multi-stakeholder Task Force and Steering Committee led by ACRP whose contributors include representation from leading industry and academic organizations across the global clinical research enterprise.

Mark Travers is the executive director of global monitoring excellence in the Global Clinical Trial Operation division at Merck. He's excited about how core competencies can be leveraged to improve clinical trials on different levels. ACRP spoke with him recently to get his take on why this shift is a critical next step toward professionalizing the clinical trial workforce to meet tomorrow's demands.

HOW WOULD A CRA COMPETENCY FRAMEWORK BE HELPFUL TO MERCK AND PERHAPS SIMILAR ORGANIZATIONS?

Travers: [The important thing is that] we can adapt our training to adopt the requirements and needs [being addressed in the framework]. What we've done is create a CRA training curriculum that matches the competencies so that, as CRAs progress within their mastery and our expectations of them increase, our training follows the competencies and we give them the tools and training to do the job.

What that means is that if you know what the competencies are to do the job, [you can ask yourself if] you have those competencies. If someone doesn't have the competencies, can we train the CRA and the CRA manager to have a much more fruitful discussion with respect to their development and their career path.

HOW IS STANDARDIZATION IMPORTANT FROM YOUR PERSPECTIVE AT MERCK?

Travers: We would like CRAs to uniformly accomplish their task when they go on monitoring visits. When you've got a global organization of maybe 1,500 to 1,600 CRAs working in about 50 countries, you need the reassurance that everybody is doing basically the same thing every day at each site. That, for me, is important for the CRA function in terms of standardizing what we expect them to do when they go on a monitoring visit or when they conduct a monitoring visit over the telephone.

We do need standardization because when we are inspected by authorities, they look at our standard operating procedures and guidelines, and they are saying to us, "Are you doing this in all of the countries at all of the investigational sites?" Without standardization, we can't really say yes or no. With standardization, we can say, "Yeah, 95% is done," and it's accomplished, and the CRAs are following our monitoring standards (following this path for all of the monitoring procedures).

CLEARLY, STANDARDIZATION OF CRA COMPETENCIES WILL IMPROVE OPERATIONS.

Travers: Yeah, I think so. [At Merck now] we have standards, we have operating procedures, we have several guidelines. I am in the newly created position of global head of monitoring excellence. This was created to bring greater standardization to the global monitoring organization, and we're beginning to do that. We're looking at processes, we're looking at procedures, we're looking at technology, and more.

I think that what we want to do is have a framework that we can refer to, but with a little bit of leeway, a little bit of customization at the country level. We have a lot of well trained and experienced CRAs, but we do have some country-level differences that we're aware of and that we support; however, the main job of the CRAs is universal in the organization.

News from the World of Workforce Innovation

Among its other timely contents, ACRP's weekly e-newsletter—the *CRbeat*—has in its short life already developed a habit for highlighting news first presented online in the ACRP Blog on the latest trends, insights, discoveries, and happenings tied to workforce innovation in the clinical research enterprise.

Presented here are excerpts from some of the recent workforce innovation items that you may have missed.

Subscribe to the free *CRbeat*
https://www.acrpnet.org/resources/crbeat

ARE CRAS READY FOR THE HIRING BUBBLE TO BURST?

Be it a stock market spike or a housing bubble, it's human nature to ride a wave without peering over the horizon to see when the crash is coming. That's true for too many in the clinical trial workforce, says Susan Romberg, vice president for global clinical development in North America at Chiltern.

"I think we've been in a long bubble, like the tech bubble, but it will change and clinical research associates [CRAs] may not be in the [employment] driver's seat" five or 10 years from now the way they are today, Romberg notes. New technologies that are already replacing the need for some site visits and drug company pressure to keep drug development costs down are likely to impact the workforce of tomorrow—shrinking that workforce even as the industry demands new skills from CRAs.

Forward-thinking CRAs would be well advised to keep pace with technology, hone their writing and research skills, and work to better understand how clinical trial data are used and moved from location to location, Romberg advises.

(Source: ACRP Blog, https://www.acrpnet.org/2017/01/17/cras-ready-hiring-bubble-burst/)

ESTABLISHED COMPETENCIES WILL DRIVE BETTER PRACTICES IN CLINICAL RESEARCH

While the demands on clinical research professionals to deliver high-quality study data more quickly and efficiently have arguably never been greater, industry continues to shy away from adapting technologies and new best practices that could help lighten the load, experts say.

"There is a lot of work to be done to manage the disparate pieces" of the clinical trial business, says Ken Getz, an associate professor and director of the Tufts Center for the Study of Drug Development at Tufts University. "There are tremendous inefficiencies and fractured collaborative efforts" slowing real forward progress, he adds.

One solution: The adoption of agreed-upon core competencies for different clinical research team roles and the overall professionalization of the industry. "It is important that we acknowledge that a focus on competency helps to drive better practices," Getz says.

(Source: ACRP Blog, https://www.acrpnet.org/2017/02/21/state-industry-established-competencies-will-drive-better-practices-clinical-research/)

REALISTIC WORKFORCE METRICS KEY TO SUCCESSFUL TRIALS

Clinical research coordinators and clinical research associates struggling under onerous workloads are likely the victims of ill-conceived trials lacking realistic workload measurements that accurately measure the knowledge and capabilities of those who actually conduct the trials, says Christina Talley, MS, RAC, CCRP, CCRC, a program director with the Office of Strategic Research Initiatives at Houston Methodist.

In their excitement to land the business, many sites say "yes, yes, yes" to everything before understanding how they can handle the project. That approach can lead to site staff burnout and sponsor frustration, or, worse, failure to successfully conduct the trial, says Talley. The key is proactively and objectively measuring site staff, she says. That means drilling down to examine each employee's credentials and, more importantly, his or her demonstrated skill sets.

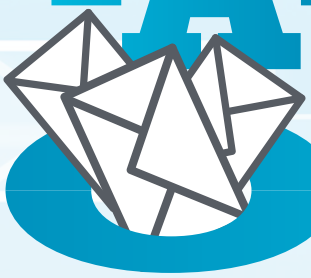
"There are many facets of employees that go way beyond" a title on a piece of paper, Talley notes. Accurate metrics, produced pre-study, can help identify gaps and assist with the placement of the right person with the right responsibilities. For smaller sites, the metrics can also be used to provide justification for the hiring of additional personnel and provide a "decision point" for hiring or rejecting a candidate.

(Source: ACRP Blog, https://www.acrpnet.org/2017/01/05realistic-workforce-metrics-key-successful-trials/)

Nicole Tesar

[DOI: 10.14524/CR-17-4011]

E-mail Overload, or the Never-Ending Game of WHACK-A-MOLE



It all begins simply enough—the sound of a gentle wave or an eager ding, or perhaps with a vibration felt from the iPhone in your pocket. Whatever form it takes, it heralds the arrival of new e-mail, and for me, it's cringeworthy. I can feel my blood pressure and heartrate rise without even knowing anything about the e-mail's contents. The reason being, each one of those e-mails represents a task to be added to an already busy schedule—something to read, a question to answer, a meeting to schedule, a request to fulfill or deny.

The fact that employees get so much e-mail every day means many of them work longer hours because so much of their time at work isn't actually spent working.

How many e-mails do you have in your inbox right now? E-mail keeps us handcuffed to our phones and computers—always alert to that distracting delivery notification of a new message because computer-mediated communication has become mainstream in work life. Whether you view this as a positive or negative in your life, it raises questions about the impact it has on our work habits and productivity.

A Day in the Life

Whether you work in an office or remotely, imagine an ordinary day on the job. You may start your morning with a cup of coffee or tea, touch base with any colleagues also arriving to begin the work day, and then the inevitable happens—you log on to your computer, and possibly for the rest of day there will be a constant inpouring of e-mails akin to a fire hose. Dealing with the deluge can be like playing a distracting game of whack-a-mole that Slows. You. Down.

Remarkably, the answering of e-mail is rarely part of our job descriptions, but more an underlying assumption of functioning in a modern work environment. Even being really good at it does not bring one bonuses or positive recommendations. Add to this the increasing use of smartphones in business, which has given the experience of receiving work-related e-mails a whole new, 24/7 dimension.

Meanwhile, many of us may find ourselves yearning for face-to-face time with our colleagues and teammates, but that's harder to pull off with more workers in remote or home offices. This is the new normal of work, and it has left people leaning on the often-dreaded e-mail even more.

The Good

It almost goes without saying that e-mail is the most widely used form of business communication, and overall it is a highly effective communication tool. E-mail is inexpensive, and it only requires an Internet connection, by which physical distance or location is no issue—in a fraction of a second, we can interact with someone on the other side of the globe.

Further, e-mail doesn't require postage and offers file attachment capabilities, making it an easy and reliable way to send documents to others. It's also more readily useful than other communication formats for rapid, one-to-many outreach, allowing users to send resources and messages with anything from simple to highly complex contents to multiple colleagues working on a team.

The Bad…and the Ugly

The fact that employees get so much e-mail every day means many of them work longer hours because so much of their time at work isn't actually spent working. The bottom line is that too much e-mail makes employees miserable; many admit the distraction of e-mail makes it near impossible to get work done, or even to socialize normally. Indeed, one position holds that, in the absence of nonverbal cues, we miss important information about attitudes, emotions, and personal characteristics, resulting in a less sociable, understandable, and effective relationships and communication.

E-mail has gotten out of control to the point where it's used for everything and anything. Today, only about one in three e-mails is essential for work. To give you an analogy, imagine trying to fix every problem in your house with just a screwdriver. You might come across a few instances where that screwdriver comes in handy, but more often than not, it's just the wrong tool.

Studies have shown that many of us suffer from "e-mail addiction," checking our inboxes as often as 30 or 40 times an hour. This drastically cuts productivity, because processing too many e-mails distracts us from the task in hand, and it can take about a minute on average for our brains to refocus on what we were doing.

Increasing expectations from managers regarding staff availability suggest that employees feel compelled to immediately respond to work-related messages, even during leisure time. Further, many staff report increased work pressure and the inability to separate and keep distance from work.

The costs of e-mail seem to be disproportionally loaded on the recipient, who has to deal with excessive amounts of e-mail and the pressure to answer these messages as soon as possible. In a related trend, smartphones can increase the flexibility of an employee, but also facilitate working longer hours with a parallel risk of disturbing work-life balance. These mobile devices can extend our job demands during the day into the evening hours, and multitasking in any setting can lead to lower quality work. When you're constantly being interrupted, your brain is not operating at its full capacity.

Just Consider

On the bright side, some companies are coming up with both behavioral and technical answers to the e-mail overload issue. For example, such video conferencing platforms as Skype and WebEx offer a humanizing complement to e-mail. Social collaboration tools like Yammer, Chatter, and others can replace e-mail for much of your team's communication and document sharing. Further, e-mail, for all its comfort, is terrible at building rapport among far-flung colleagues, whereas chatrooms within social collaboration tools excel at this relationship building.

Other options are to cure your e-mail addiction by checking that inbox less often; however, very few people have the discipline to structure their days in such a way as to only deal with e-mails at fixed times. If you are able to check your e-mails, say, twice a day, then it's also worth doing so at set times. One rule of thumb is to never check e-mail in the morning, on the grounds that doing so distracts you from higher priority work at a time when most of us are in our most productive state of mind.

Meanwhile, most companies are good at discouraging the use of the "reply all" feature, which generates lots of extra e-mail, and some companies are recognizing the burden of e-mails and implementing "e-mail-free Fridays."

Conclusion

Although we will likely never escape the burden of e-mail all together, you should find what works for you so that you do not experience "tech stress" as you try to do your job well while also enjoying balance and the ability to shut down at the end of the workday. For me, I have learned that to get "real work" done, I now have to shut down Outlook and turn off my iPhone.

Nicole Tesar (ntesar@harmonyclinicalconsulting.com) is owner and director of clinical operations with Harmony Clinical Consulting Corporation in Avon, Ohio.

TWO CONFERENCES FOR THE PRICE OF ONE

Complimentary access to SCCE's Higher Education Compliance Conference is included with your registration.

Register by April 11

SAVE $300

Research Compliance Conference

June 4–7, 2017 | Baltimore, MD

Join us for the primary education and networking event for research compliance professionals. Increase the effectiveness of your compliance program, discuss emerging risks, share best practices, and build valuable relationships.

HCCA
HEALTH CARE COMPLIANCE ASSOCIATION

hcca-info.org/research

QUESTIONS? catherine.stollenwerk@corporatecompliance.org

FXM RESEARCH

IT'S NOT JUST CLINICAL RESEARCH!

IT'S CLINICAL RESEARCH EXCELLENCE... SUSTAINED!

Founded in the year 2000, **FXM Research** is a privately owned and operated Clinical Research Site that conducts phase II, III, and IV clinical research trials specializing in Dermatology. Throughout the years, our ability to deliver aggressive, time bound enrollment goals, while providing trustworthy data to Pharmaceutical companies and CROs, has earned **FXM Research** a great deal of notoriety and fame within the Dermatology research industry.

Today, FXM Research's success is widely regarded throughout our four operating branches: **FXM Research Corp.**, based in Miami, Florida and home of our headquarters, **FXM Research Miramar**, located in the city of Miramar, Florida and **FXM Research International**, including two branches in Belize City, Central America.

OUR MISSION

At the core of our business and operating systems, **FXM Research** mission is to support pharmaceutical companies and CROs with introducing new and approved FDA medications successfully into the marketplace. We perform this efficiently and effectively by providing the highest quality service in a timely fashion and at the lowest possible cost.

- We specialize in conducting phase II, III, and IV Dermatology Clinical Trials.
- Our primary concerns are subject safety and adherence to the protocol.
- Turnover time for Regulatory Documents, budgets, and contracts is usually 24 to 48 hours.

OUR SUCCESS

- We offer experienced, trained, and bilingual personnel (English and Spanish), who interact with our subjects, sponsors, and CROs as a cohesive team.
- Our Principal Investigators are Board Certified Dermatologists and Certified Clinical Research Investigators with many years of extensive experience. They are located onsite and are available full-time.
- Most subjects are recruited from the office of our PI's private practice, and/or FXM Research's extensive clinical database. We draw heavily from a Spanish speaking population, a group often under-represented in clinical trials. We also have continuing extensive experience with a pediatric population.
- We do whatever is necessary to accommodate our subjects' school and/or work schedule, which maximizes compliance and retention.
- We are confident that we can surpass sponsors expectations relating to cost, subject enrollment/retention, and the quality of our work.

TO CONTACT US

Francisco Moncada, R.N., B.S.N., C.C.R.C., President & Director of Clinical Research
Email: info@fxmresearch.com • www.fxmresearch.com

FXM Research Corp.
Hector Wiltz, M.D., C.C.T.I.
(305) 220-5222 Office
(305) 220-5779 Fax

FXM Research Miramar
Francisco Flores, MD
(954) 430-1097 Office
(954) 430-5502 Fax

FXM Research International – Belize, Central America
Julitta Bradley, MD & Ines Mendez-Moguel, MD
(305) 220-5222 Office
(305) 220-5779 Fax