

# Employing Secure Online Site Initiation Practices to Accelerate Subject Enrollment

*How to Ensure Data Integrity Using Advanced Compliance Management Technology*

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The cost of developing a new drug or medical device has become overwhelming, with time to market and development costs continually increasing. With these ongoing challenges, even the most successful pharmaceutical, medical device company has a solid business imperative to identify and employ any opportunity to reduce the cost and time of new product development.

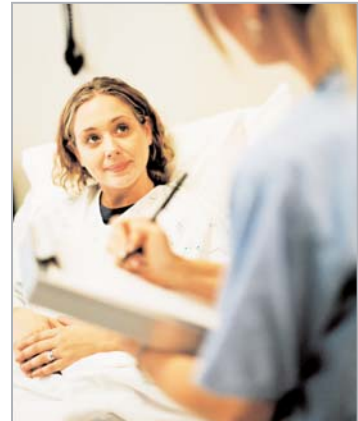
Clinical trials, which can include hundreds of patients and multiple study sites, represent the costliest and most time-consuming phase of product development. Even short delays in bringing medical products to market, whether a blockbuster drug or an implantable device, easily translates into millions of dollars in lost sales.

The development of new medical treatments and products can never be risk-free. Although many delays or cancellations are triggered by science, others are the result of clinical trial management and compliance issues. These delays can be avoided with an effective strategy that ensures regulatory compliance, study efficiency and research integrity, while delivering the additional benefits of cost-efficiency and trial acceleration.

## In the Crossfire

Today's clinical trials are more complex, regulated and scrutinized than ever before. Their complexity increases in direct proportion to the depth and scope of medical knowledge and innovation. Demanding regulatory requirements set a baseline for knowledge and documentation throughout the study, as well as the growing reliance on global study sites, adds new layers of

regulation by national and regional agencies. Exacerbating these hurdles is the complicated relationship between the life science industry and the public, in which a growing demand for ever-more sophisticated medical treatments is counterweighed by deep concern over product safety and corporate ethics.



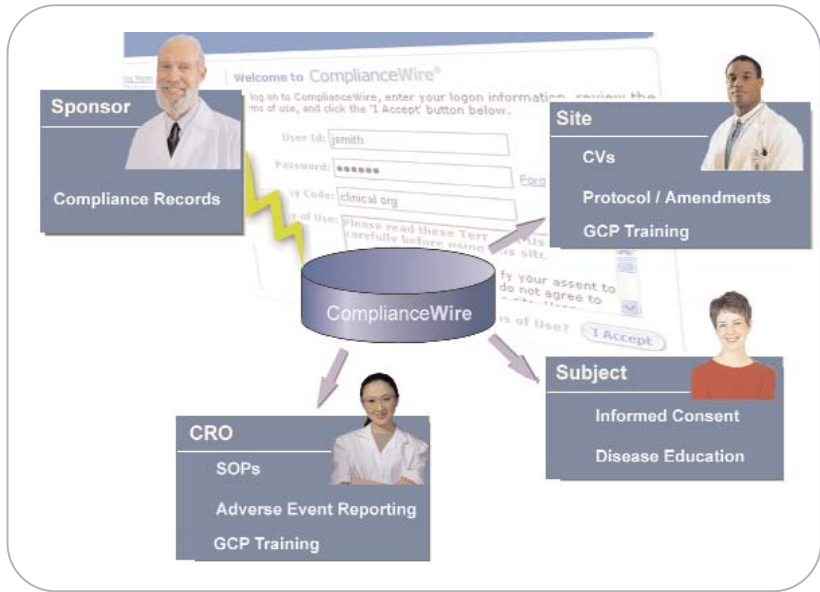
Standing in the crossfire of these factors, the pharmaceutical and medical device industries face a litany of additional issues that impact clinical trials. Two challenges are particularly important during a time when as many as 50,000 clinical trials are underway in the US alone: the availability of experienced investigators and the population of potential study participants.

The Center for Information & Study on Clinical Research Participation quotes findings by CenterWatch that 80% of US clinical trials are delayed at least one month due to unfulfilled enrollment. At the same time, the number of principal investigators conducting industry-sponsored clinical studies in the US showed a disturbing drop of 11% in the first five years of this decade, with nearly half declining to participate in a subsequent clinical study. According to Ken Getz, author of a Tufts Center for the Study of Drug Development study into the drop in investigators, "The capacity of the market to conduct clinical trials for industry sponsors is eroding and efforts to establish a well

trained, experienced pool of clinical investigators may become more difficult.”

## The Costs of Non-Compliance

While much attention focuses on the costs of patient and investigator recruitment on clinical trials, noncompliance with regulatory requirements represents one of the most significant – and unnecessary – risks to a clinical study’s research integrity and bottom line. Sponsors of clinical trials shoulder the ultimate responsibility of regulatory compliance. Inadequate knowledge among clinical investigators and support staff, investigational review boards, and corporate compliance personnel can delay or derail clinical studies, regardless of their location. In fact, inadequacies at only one site in a multi-location study can compromise the entire study and postpone or prevent product approval by regulators.



*A clinical compliance management system, such as ComplianceWire, links all study team members and ensures that they can fulfill their interrelated responsibilities; the centralized platform distributes and documents receipt of critical clinical study knowledge.*

Regardless of a study’s location, the sale of the medical product in the US requires FDA approval of study results and compliance with FDA-mandated standards of knowledge, critical information management and documentation. A quick look at recent 483s and Warning Letters issued by FDA illustrates the frequency with which these requirements are not met and the costly, time-consuming follow-ups required of noncompliant practices. Scrutiny of clinical trial compliance is likely to intensify as highly

publicized recalls place the FDA in the crossfire of questions about drug safety, noncompliance enforcement and the FDA approval process. Additional clinical risks include failures in providing timely and consistent updates of critical study information to both the internal and external study teams, assurances that the study and product information was received and understood by the responsible person, and failure to start or complete post-marketing commitments on time.

### Accelerating Site Initiation

**Background:** A leading human therapeutics company for more than two decades, this Fortune 500 company is widely recognized for commitment to innovation, patient safety and operational efficiency. To accelerate site initiation across 60 clinical trials in 2006, the company implemented ComplianceWire®, Kaplan EduNeering’s clinical compliance management system. Study participants from around the world were trained on study protocols and EDC operations, with proficiency tested and documented using ComplianceWire. Based on that proficiency, access to the EDC system was enabled, ensuring the integrity of trial data because only trained personnel were able to enroll patients.

**Results:** The time required for site initiation was cut from 6 weeks to 3 days, while accelerating subject enrollment and reducing training costs.

## Global Training to Assure GCP Proficiency

**Background:** The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, is one of the world's leading medical research organizations with research partners and study sites around the world. ComplianceWire serves as the foundation of NIAID's comprehensive, global knowledge initiative to ensure proficiency of all responsible parties around the world. ComplianceWire will distribute, validate receipt and understanding, provide an audit trail, and document proficiency through computer-based courses and standard operating procedures in subjects including informed consent, research ethics, drug safety and adverse event reporting. The comprehensive learning solution enables NIAID to assure compliance and proficiency, respond quickly to identified knowledge gaps, and manage all learning activities throughout its network of facilities, partners and grantees.

**Results:** Proficiency in good clinical practices is crucial to NIAID, which requires that any recipient of a NIAID research grant, their study staff and key NIAID personnel be trained in Good Clinical Practices.

## Beyond Process Improvement

Productive, efficient companies have embraced process improvement systems to more effectively manage the global supply chain. These systems have frequently produced substantial business benefits across the unique "supply chain" of knowledge and compliance in a clinical trial. Like their process improvement counterparts, clinical knowledge management systems streamline critical functions.

To be effective, a clinical knowledge management system should incorporate specific capabilities, including:

› Internet-enabled technologies, which enable simultaneous global distribution, receipt and documented comprehension of clinical study knowledge including:

- study protocol
- subject selection criteria
- informed consent
- GCP/ICH obligations
- adverse event reporting responsibilities

› Secure, validated infrastructure that enables electronic communication with all external study personnel, overcoming the challenge of opening up a sponsor's internal firewall to a myriad of external parties;

› Interoperability with the sponsor's existing infrastructure, including EDC, document control and clinical trial management systems, enabling a seamless process to "communicate" with external clinical team members;

› Identification of knowledge gaps, generation of targeted training, and monitoring of the required behavior change throughout the duration of the study via testing and certification; and,

› Creation of easily available, audit-ready documentation for compliance purposes.

## Meeting Expectations

The pressures facing the drug and medical device industries, both financial and scientific, will not ease. Rather, they can be expected to intensify with the growing challenges of generic and counterfeit products, inconsistent regulatory requirements in developing nations, competition among companies to be the first to market, and the growing knowledge demands of today's clinical research. To succeed in that competitive and demanding environment, all team members must be able to fulfill their regulatory and study responsibilities. By ensuring that performance, potential delays can be avoided and cost efficiencies can be maximized.

## Delivering Cost Efficiency

**Background:** A fast growth pharmaceutical company began trials on several new indications and needed to develop an alternative approach to in-person investigator training meetings. In the past, each meeting cost thousands of dollars, required significant travel and time, and resulted in inconsistent retention of critical knowledge among investigators and study coordinators. Additionally, the company wanted to expand their recruitment of qualified, trained investigators outside the U.S. ComplianceWire was introduced to deliver study documents, administer GCP training, and test on SOPs. Users were given the opportunity to “self-register” via Kaplan EduNeering’s secure server, enabling rapid initiation of site personnel.

**Results:** A 40% reduction in site initiation training costs was recognized, while proficiency on the study material was tracked and measured.

## Focusing on Results:

### *What Can a Clinical Knowledge Management System Do?*

Although each member of a clinical team — sponsor, monitor, CRO and investigator — is subject to specific regulatory and study requirements, the study's sponsor is ultimately responsible for the trial's design, staffing, performance and compliance. An effective clinical knowledge management system supports compliance throughout the team, assisting sponsors to minimize delays in study initiation and patient enrollment, by assuring that study team members have completed mandatory training before performing study procedures.

› **Study Initiation:** For a clinical trial to launch successfully, any knowledge gaps of study personnel must be identified and mitigated through a rigorous process that determines competency and provides remedial or adjunct training. Within and external to the sponsor's organization, all responsible parties including study management, research coordinators, monitors and investigators must be knowledgeable about prevailing requirements that range from the GCPs to HIPAA compliance, informed consent and study protocol. Any compliance management system should include an objective assessment tool that enables sponsors to confirm the study personnel's understanding of key study knowledge and obligations.

› **Ongoing Learning:** Industry reports indicate that up to 60% of the delays associated with clinical trials can be traced to inadequate knowledge among study participants. Consistent and timely study initiation is a critical component of study efficiency and compliance. Frequent staff turnovers, changing study protocols and regulatory requirements, and any identified failures in job performance should trigger new-hire and/or refresher training and, when necessary, remedial training. A

system for quick and accurate identification of inadequate knowledge is critical for required tasks ranging from subject eligibility to adverse event reporting and precise study procedures. Equally important, systems must enable ongoing assessments to ensure that the training produces the true behavior change needed to achieve compliance and quality data.

› **Critical Information Control:** Any clinical trial is an information-rich endeavor with fast-changing knowledge requirements. All team members must be able to receive, validate receipt, and confirm understanding of critical information ranging from standard operating procedures to GCP requirements, and changes in study protocol. Electronic technologies can improve the reliability, accuracy and receipt of critical information through e-signatures, mandatory validation, individualized forms to confirm understanding, and storage of documentation in audit-ready formats.

› **Secure, Audit-ready Documentation:** Part-11 validated infrastructure that securely networks all external study sites with the sponsor is of ever-increasing importance as study sites become more dispersed and distant. A clinical knowledge management system that can securely connect authorized, dispersed investigator sites overcomes the challenge of opening up a sponsor's internal firewall to a myriad of external parties.

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