ScienceMedia

SMi Trial™ Training Resource

Eliminate Protocol Deviations from Your Clinical Trials!

How to effectively improve patient safety, increase data quality, and reduce trial costs through Protocol-Specific Training.

The opportunity to avoid protocol deviations in clinical trials is something of a Holy Grail in clinical development, but for companies that are willing to invest in protocol-specific training, the quest may be less frustrating and futile. This white paper outlines some of the current challenges to running trials with fewer errors—including current causes of failure and newly standardized regulations around training. Then we offer actionable solutions for drug developers in Clinical Research Organizations (CROs) and pharmaceutical companies looking to mitigate risk and lower their failure rates.

Introduction: Train to Succeed

We'd all love the opportunity to banish protocol deviations from our clinical trials, and in theory, it can be done! Certainly, those deviations should be rare but given the increasing complexity of trials, the massive number of data points now being collected, and the need for more regulatory oversight, it's clear that avoiding costly deviations requires vigilance and education.

Protocol deviations can occur during any clinical trial, at any time. Deviations may be caused by the investigator or study staff, or they may be subject related, and they may occur because of misunderstandings about expectations during the trial or specifically how to operationalize parts of the approved protocol. Still, there are many ways to help mitigate and avoid protocol deviations. One way is to start with a protocol that is clearly written and approved by an Institutional Review Board (IRB). Prior to initiating the protocol, have a comprehensive understanding of the disease, population, and the investigational drug/device under study so that the protocol can be as detailed as possible (i.e. train to succeed). This will help sort out any potential questions while the study is underway and facilitate smooth interactions between study staff and subjects. The protocol should clearly identify the study inclusion and exclusion criteria so that the proper study population is enrolled from the start.

Ensuring that all members of the study staff working on the trial are trained and qualified is a prerequisite. They should be well versed in good clinical practice guidelines, institutional (particularly IRB) policies, and study visit procedures. Assessments should be performed to determine whether the study team members have been properly trained on their roles within the study and on how to perform designated tasks. Additional training, or retraining, should be provided in real time, as needed.

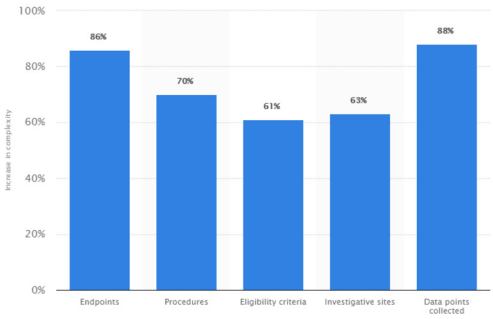
> **"Project specific training, however, should be provided for CRAs whether they are employed or Independent and can be delivered by the CRO and/or the pharma company. This type of training should be customized to ensure understanding of the protocol and the disease which is being investigated…The workload and pace for CRAs are greater now than it has been in years past and with the addition of clinical trials being more complex, it requires a broader understanding around the disease and treatment."**
>
> *Miseta E. "Is There A Solution to The CRA Shortage Problem?" Clinical Leader. January 4, 2018.*

Lack of mutual understanding and respect often leads to communication and trust issues in any working relationship. If this happens in a clinical trial, the site personnel may shy away from that particular protocol, resulting in low enrollment; or they may not fully understand the intricacies of the protocol, resulting in protocol deviations that are found late in the trial. Conversely, a CRA often does not understand the intricacies of a disease, patient care and journey, and clinical practice, which the site personnel know as second nature. Though the CRA is an expert on the protocol, lack of effectively training site personnel to this level leads to protocol errors and inclusion or omission of appropriate study participants. Rectifying this knowledge gap requires educating the site, which takes more time and further delays the study.

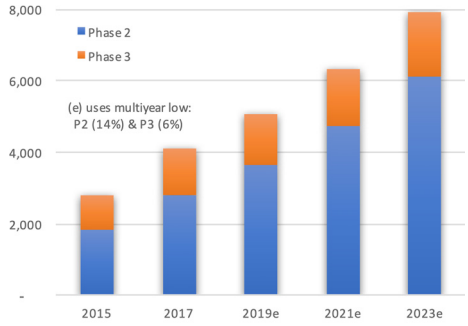
ScienceMedia has offerings that address knowledge gaps. This article addresses a new approach to educating sites on the high-risk items within a protocol.

1. Increasing complexity of clinical trials

From almost all perspectives, clinical trials are getting more complex. Studies that compared various complexity metrics for clinical trials conducted in 2001–2005 versus those in 2011–2015 show, on average, that trials are 60% more complex. In the accompanying figure, the number of endpoints collected is up 86%, procedures are up 70%, and eligibility criteria are up 61%.



As the complexity of trials increases, so does the number of trials. In the accompanying figure, the historical and projected number of trial starts in the U.S. increases annually by more than 10%. In five years, we expect twice as many trials as today and four-times the number of trials as just five years ago.



(clinicaltrials.gov)

Yet, with all the effort focused on improving efficiency of clinical trials, the time to complete a trial remains nearly constant. U.S. trials still fail to meet patient enrollment goals two thirds of the time, thereby requiring more sites to be recruited around the world.

2. Protocol training: current practice

Training your site personnel on a 100-page protocol often means providing an accompanying 100-slide PowerPoint deck to the PI and study coordinator at an investigator meeting and then again at site initiation visits. The problems with this approach are well known.

- All aspects of the study are treated equally; no special emphasis on highest risks for protocol deviations.
- Some material is redundant to prior studies that the site personnel has been trained on.
- The most significant training is at the investigator meeting, but other critical site personnel are not present. Subsequent training is passed down—the CRA, to the study coordinator, to functional personnel (e.g., pharmacists)—thus training consistency diminishes.
- New hire training then requires a site visit, so onboarding personnel slows the trial.
- PowerPoint presentations, whether delivered live or via Webinar, are well documented to be only marginally effective as a training delivery approach. Within weeks post-presentation, their value is almost completely lost.
- All training is upfront, often months before aspects are needed. Subsequent, quick access to the relevant material at a given stage in the trial is difficult.

> **"Training is general, impersonal & not designed to address individual learning needs."**
>
> *VP Quality, The Medicines Company*

3. Relevant ICH GCP E6(R2) Regulations

"The need for training and ongoing quality improvement is stressed in the revised International Council on Harmonisation, E6(R2)…however, despite mandated training, FDA inspection results remain static and deviations related to informed consent, eligibility, adverse event reporting and endpoint collection continue to occur at higher than expected rates." [Jones C, et al. "A retrospective pilot study comparing data from monitoring reports to identify staffing influence on protocol deviation rates." *Int J Clin Trials*. 2018 Feb;5(1):30-36.]

The FDA and EMA have embraced these changes in order to encourage improved approaches to trial conduct, recording, and reporting. Much of the press around these changes relate to risk-based monitoring. Once the highest-risked aspects of a protocol are identified, then a risk mitigation plan is needed. Aspects include:

- Emphasized training focused on the highest risks for protocol deviation
- Measuring and recording the site personnel's understanding of the protocol

> **"With the complexity of current trials, it is more important than ever to ensure research sites are well trained and truly comprehend the indications & protocols.**
>
> *EVP, PRA Health Sciences*

Further, the Clinical Trials Transformation Initiative (CTTI) has issued draft guidance regarding site training that states the training should be:

- Targeted to trial, role, and experience
- Self-directed, just in time, practical, and relevant
- Placed in a platform to record completion and understanding

"Ensure CRAs are well trained on your protocol. They should know the protocol in detail. They should be able to answer common questions, and also know how to access answers to less common questions that arise. If every CRA is well versed in your protocol, the loss of one of those individuals will be less disruptive to your study. If your protocol is well known to just one key CRA, their loss can bring your study to a crawl." ["3 Ways to Manage Excessive CRA Turnover." *Clinical Leader*. June 8, 2016.]

4. SMi Trial: A Better Way to a Deviation-Free Trial

SMi Trial is an offering from ScienceMedia used to train site personnel on the protocol items that are deemed to have the highest risk for deviation. In contrast to the standard PowerPoint approach, SMi Trial:

- Focuses on the key potential problems. For one protocol it could be inclusion criteria, another may be sample management, and a third may be the timeline of steps over multiple patient visits.
- Eliminates the variance of training given by multiple people with interactive, instructionally developed, multimedia material that keeps the learner engaged, and improves comprehension and retention.
- Available 24/7 through brief microlearning segments, which enable training when and as needed during a trial, and as new personnel onboard.
- Assesses understanding of the trial by all site personnel so that an auditable record is stored and so that misunderstanding is identified early to focus additional training where needed before deviations occur.

5. Experience with SMi Trial: Real improvements that create measurable benefits

One global CRO has mandated SMi Trial for all Phase 2 and Phase 3 trials. The CRO uses a training format that is slightly less than two hours in duration and addresses:

- Disease and Treatment: Describe disease, progression, symptoms, and types, and list diagnostic criteria. This could be tied to differences in the trial regarding standard of care; or, it could focus on diagnosis, or when one may enroll subjects in the wrong arm.
- Therapy: Introduce investigational therapy. Current treatments and disease management approaches. Particularly useful with trials of new molecular types or modalities (i.e. CAR-T, immunoncology)
- Protocol: Protocol design. Sample size. Blinding procedures and randomization. Primary endpoints. Dose regimen. Key I&E criteria. Schedule of visits and assessments. Study procedures. Questionnaires, scales, and diaries. Minimizing placebo effect. Links to patient and staff-specific videos. Recruitment.
- Product: History of investigational therapy and MOA. Form. Supply chain. Storage. Protocol-specific equipment and transport of data.

In one Phase 3 study, the CRO chose to use SMi Trial globally after seeing enrollment mistakes and confusion regarding procedures at specific patient visits, when the trial was initially deployed in the U.S. SMi Trial was deployed in this rescue study, providing reinforcement training at 48 of 142 active global sites, for 287 site personnel and 40 CRAs. Collaborating with the study's CTMs, ScienceMedia designed the training to reinforce key competencies, such as the study's complicated dose regimen. Further, the training's associated scored assessment revealed a key misunderstanding related to subject visit windows. Accordingly, CRAs discussed this topic at sites with incorrect responses and the trial subsequently experienced minimal protocol deviations, globally.

6. Some results

EVP Medical Affairs "SMi Trial leverages industry leading approaches to improve retention & comprehension, and **will improve trial compliance & performance."**

Sites "…the format is a refreshing solution that allows training to be developed that provides interest and education, allowing the key elements of the study to be emphasized and most importantly, **easily facilitates tailored education based on role and level of experience."**

Operations "The multimedia format was **by far the best approach** as it enabled us to convey & reinforce specific objectives for our complex program.

The training modules provided our team foundational knowledge and details about study endpoints and **objectives, which could not be easily drawn from the protocol, IB, or other core documents."**

- SMi Trial has been successfully deployed in over 30 Phase 2 and Phase 3 trials during 2018.
- Proactively minimized potential protocol deviations.
- Site staff now have access to trusted, on-demand reinforcement training from any location.
- Auditable verification of training completion, ensuring CRO and sponsor training GCP obligations are met.
- “Extremely positive” feedback, with sites delighted to have an enduring, easily accessible resource that highlights problem areas of the study, rather than having to rely on lengthy protocol documents.
- SMi Trial helps sites, CROs, and sponsors achieve the overall goals of improved patient safety, increased data quality, and reduced costs.

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About ScienceMedia & SMi Trial

For nearly 25 years, ScienceMedia has been delivering innovative learning solutions aimed at improving clinical competency throughout life sciences' R&D, clinical, medical affairs, and commercial organizations worldwide.

SMi Trial is a cutting-edge solution proven to significantly improve and optimize clinical trials of biopharma and CRO organizations through the delivery of effective, protocol-specific training.