RESEARCH PRACTITIONER

November–December 2023



# Studies within trials evaluate, improve clinical trial processes and tasks

*by Elizabeth Tilley Hinkle*

The efficiency and effectiveness of clinical trial procedures is central to generating accurate safety and efficacy data from those studies. Critical processes such as participant recruitment and retention can affect how well a trial operates to meet its goals.

Increasingly, research teams are combining the best of both worlds with a tactic called study within a trial (SWAT), piggybacking on existing study infrastructure to test their protocols and processes with an eye toward improving future studies.

"Clinical trials often fail to reach their endpoints and low participant enrollment remains a critical problem with trial conduct," Kristian D. Stensland et al. write in *Implementation Science Communications*.[1] "Clinical trials [are] beneficial evidence-based practices suffering from poor implementation."

SWATs can help researchers address those implementation problems by helping principal investigators (PI), study coordinators and other members of the clinical research team evaluate the effec-

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Learner Outcomes:

1. Describe the benefits of studies within a trial (SWAT).
2. Explain best practices for conducting SWATs.
3. Discuss how SWATs can improve recruitment and retention.
4. List other types of queries that are suitable for SWATs.

# Assessing new clinical research investigators, study coordinators during site evaluations

*by Elizabeth Weeks-Rowe, CCRA*

Identifying and evaluating investigational sites is one of the most critical aspects of study startup. A clinical trial can't commence without it. The final site list is determined by a rigorous site evaluation process to assess whether there are appropriate facilities and equipment and qualified personnel necessary to conduct a study.

In a prestudy evaluation, also called a site qualification visit, a clinical research associate (CRA) examines the research infrastructure to ensure patient safety, credible data and overall potential for successful participation.

They also interview principal investigators (PI), study coordinators and ancillary staff to determine their experience, workload and to glean further insight into training policies. Ensuring all research team members, especially those in leadership roles, are prepared for the visit is paramount for making a good impression. And this is especially true when new investigators, coordinators and other recent hires are part of the overall site assessment.

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Learner Outcomes:

1. Discuss the focus on new staff during site evaluations and why it's important.
2. List examples of queries to evaluate preparedness of new personnel.
3. Describe evaluation queries that can uncover often-overlooked qualifications.
4. Summarize how sites can prepare new employees for successful site visits.

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- Apply ethical and legal principles for the conduct of research and the protection of human research subjects; and
- Conduct clinical trials to comply with U.S. and global regulations.

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# Regulatory Update

Contact hours not offered for these articles

## Biomarkers Pinpoint Immune Dysfunction in Patients with GVHD, FDA Guidance Says

Developers of graft-versus-host disease (GVHD) therapies can design trials based on a new FDA draft guidance that focuses on using biomarkers to identify individual patients' specific immune dysfunction rather than suppressing the entire immune system.

Traditional treatment of GVHD has depended largely on drugs that impair T cells, the FDA says, often resulting in "profound immunosuppression." But recent research has helped identify other components of the adaptive immune system that can be targeted.

The 39-page draft guidance, "Graft-versus-Host Diseases: Developing Drugs, Biological Products, and Certain Devices for Prevention or Treatment," applies to development of drugs, biologics and certain devices to prevent/treat acute and chronic GVHD occurring after allogeneic hematopoietic stem cell transplantation.

The guidance covers overall clinical development and design elements for early- and late-phase trials and delves into drug combinations, efficacy endpoints for prevention/treatment of acute GVHD and treatment of chronic GVHD, and recommendations for raw data submitted in marketing applications. It is not intended to provide advice on the technical aspects of therapeutic or cell-processing devices.

Read the GvHD guidance here.

## New FDA Draft Guidance Pushes for Development of Stimulant Use Disorder Treatments

With no FDA drug approvals to date for stimulant use disorder, the FDA has published draft guidance outlining current recommendations for development programs and trial designs of moderate-to-severe cocaine use, methamphetamine use and prescription stimulant use disorder.

The 14-page draft guidance offers the latest agency thinking on early phase development, efficacy trial considerations, endpoints, benefit-risk considerations, labeling, and the use of expedited programs for stimulant use disorder treatments, though ever-changing evidence and continued FDA research in this area means the recommendations aren't likely to remain static.

The FDA cautions sponsors about prospective challenges when it comes to designing trials to evaluate the safety and effectiveness of stimulant use disorder drugs, including selecting trial populations and choosing the most appropriate clinical endpoints.

The guidance also notes the strong heterogeneity of patients meeting DSM-5 criteria for stimulant use disorder and the resulting challenge of identifying drugs that are effective for the whole subset of patients diagnosed with cocaine/methamphetamine use disorder and patients meeting the broader criteria for stimulant use disorder. It also calls out the differing drug mechanisms between cocaine, methamphetamine and other stimulants that can contribute to differences in clinical presentation and treatment responses among patients as another challenge.

Read the full guidance here.

## UK Accelerates Review Times for Postmarket, Certain Phase 3 Trial Applications

Sponsors of postmarket trials and certain phase 3 trials can now expect the UK's Medicines and Healthcare products Regulatory Agency (MHRA) to process their trial applications within two weeks rather than the statutory 30 days, as long as they meet certain criteria.

The accelerated review times, part of the UK's efforts to revitalize its clinical research ecosystem and make conducting trials in the country more attractive to sponsors, apply to lower-risk postmarket trials and phase 3 trials.

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This accelerated process does not yet apply to phase 1 trials, phase 2 trials or protocol amendments, the MHRA noted.

"Clinical trials regulation should be flexible and risk-proportionate so that the regulatory requirements are geared to the risk that a trial presents," June Raine, chief executive of the MHRA, said. "[This] will reduce the time taken to get the lowest-risk clinical trials up and running without undermining patient safety."

For postmarket trials, two criteria must be met:

- The trial's investigational product(s) must be licensed and used according to the relevant UK, U.S. or EU approval, except for placebo; and
- There must be no ongoing safety concerns regarding the investigational product(s) that the sponsor is aware of, such as other trials on clinical holds, other trials with unresolved urgent safety measures or postmarket regulatory restrictions.

Phase 3 trials must meet at least one of these criteria:

- The trial is already approved in the U.S. or EU based on the same protocol and investigator brochure submitted to the MHRA, and for the EU, the same version of the investigational medical product dossier. For trials solely approved by FDA, the dossier submitted to the MHRA must include the same investigational product manufacturing process.
- The MHRA has approved, in the past two years, a prior phase 3 trial of the investigational product(s) for the same (or higher) dose, dosing (or higher dosing) frequency and indication even if the trial was with a different sponsor. This trial must also have used the same investigational product manufacturing process.
- The investigational product(s) are approved and used according to the relevant UK, U.S. or EU approval, except for placebos.

In addition, accelerated review times do not apply to phase 3 trials with complex/innovative designs (such as basket, umbrella or platform trials) that allow for prospective major changes, pediatric patients, pregnant or breastfeeding participants, first-in-class investigational product(s), or investigational product(s) that are advanced medicinal products.

Register for the new review process here.

## EMA Simplifies CTIS with Revised Data Transparency, Sponsor Deferral Rules

The European Medicines Agency (EMA) has revised the data transparency rules for its Clinical Trials Information System (CTIS), reducing complexities and barring sponsors from deferring the publication of critical data and trial documents.

The revised and simplified data transparency rules, which "strike a balance between transparency of information and protection of commercially confidential information," according to the EMA, will better serve patients by ensuring that trial information most relevant to them is published early. In particular, it will help improve the user experience for multinational trials, which require sponsors to provide many documents.

The revisions also make it easier, procedurally, for sponsors to protect participant data and commercially confidential information, and for healthcare professionals to navigate the system and access information about trials, enrollment and potential treatment options, the EMA says.

The new rules remove deferral capabilities for every trial category, which had allowed sponsors to delay the sharing of key trial documents, including protocols, for certain types of trials for up to seven years after a trial ended. As part of this, the updated rules narrow the publication of documents to only those most critical to patients and researchers.

The EMA said it is working to fully implement the new rules by Q2 2024. CTIS users will be alerted prior to the rules becoming applicable.

Read the revised data transparency rules here.

## CDER Seeks Industry Feedback on Clinical Trial Innovation

Seeking to better understand innovative clinical trial designs and approaches, the FDA's Center for Drug Evaluation and Research (CDER) has asked stakeholders to share their thoughts on the current barriers to and enablers of innovation.

Feedback submitted to CDER will help inform future actions on trial innovation as well as an upcoming public workshop hosted jointly by FDA and the Duke-Margolis Center for Health Policy. The workshop, scheduled for March 19-20, will delve into such topics as regulatory/compliance, patient-centricity/recruitment and trial infrastructure/organizational culture.

The deadline for submitting feedback to CDER is April 19. Submit comments here.

Register for the workshop here.

## Two FDA Guidances Present Technical Specifications for Clinical Trial Data

The FDA has issued a pair of final guidances meant to assist sponsors with submitting patient-reported outcome

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(PRO) data gathered in cancer trials and general clinical outcome assessment (COA) data, respectively, offering t echnical specifications.

In the 20-page final guidance, "Submitting Clinical Trial Datasets and Documentation for Clinical Outcome Assessments Using Item Response Theory," the FDA provides technical specifications for submitting COA data that uses Item Response Theory (IRT), a family of mathematical models that describe "the functional relationship between item performance, item characteristics and the patient's status on the construct being measured."

Specifically, the guidance covers static, fixed-length COAs that are developed and/or scored using IRT and COAs that are administered using IRT-based Computerized Adaptive Testing, a type of individual testing done by a computer "in which successive items in the COA measure are selected for administration based primarily on the item's psychometric properties and content in relation to the patients' responses to previous items."

The agency notes that the final guidance is meant to supplement CDER's Patient-Focused Drug Development (PFDD) Methodological Guidance Series.

In the separate 43-page final guidance, "Submitting Patient-Reported Outcome Data in Cancer Clinical Trials," the FDA provides technical specifications for submitting PRO data from cancer trials used to support a marketing application for an oncological medical product. According to the FDA, the technical specifications are meant to apply to any PRO data used to evaluate safety/tolerability or clinical benefit in randomized oncology trials.

The guidance includes specifications for the Clinical Data Interchange Standards Consortium (CDISC) Study Data Tabulation Model (SDTM), which sponsors are advised to use in support of PRO data tabulation, and the CDISC Analysis Data Model (ADaM), which sponsors should use to support PRO data analyses.

The agency said this final guidance supplements an FDA draft guidance from June 2021, "Core Patient-Reported Outcomes in Cancer Clinical Trials," as well as the PFDD guidance series.

Read the final guidance, "Submitting Clinical Trial Datasets and Documentation for Clinical Outcome Assessments Using Item Response Theory," here.

Read the final guidance, "Submitting Patient-Reported Outcome Data in Cancer Clinical Trials," here.

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tiveness and efficiency of trial operations and procedures with the same critical eye that is applied to safety and efficacy data.

### How to conduct a study within a trial

A SWAT is a self-contained research study that is embedded in a host clinical trial for purposes of evaluating or exploring alternative ways of delivering or organizing a particular trial process, such as recruiting study participants, retaining them, gathering informed consent and reporting study findings.

Jennifer Lai et al. note in *Therapeutic Innovation & Regulatory Science* that SWATs offer a way to generate evidence on how efficiently clinical trials operate by examining specific trial processes from that perspective.[2]

"Future research should generate evidence that demonstrates which clinical operations methodologies improve efficiency," they write, "to avoid the waste of precious resources."

Shaun Treweek et al. published guidance on SWAT application in *Trials* that outlines its key features:

- It is embedded within a host clinical trial;
- It does not affect the scientific integrity, rationale or outcome measures of the host study;
- It is designed to resolve uncertainties about a process used in trials;
- It has its own formal protocol;
- It can be evaluated in a single clinical trial but is also suitable to run across multiple host trials, either at the same time or sequentially; and
- It can provide data to inform the design and conduct of future trials and the ongoing host trial.[3]

To date, however, only a small number of such studies have been done, so there is scant evidence to support well-informed decisions about changes to clinical trial processes. One example is evidence supporting different patient recruitment strategies, "despite recruitment being a recognized problem for many trials and being identified as the top priority for research into trial methods," Treweek et al. add.

"This means that researchers doing trials, funders paying for them and patients taking part in them cannot always be sure that the way the trial is being done is as effective and efficient as it could be," they say.

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## How to prepare for a successful SWAT

SWATs can be an important methodology for understanding and refining the implementation processes of complex information, Sadia Ahmed et al. write in *Research Methods in Medicine & Health Sciences*.[4] But researchers must exercise caution, they add.

The goal of any SWAT should be to embed it without compromising the scientific integrity of the host trial. For instance, logistical issues could affect how readily a SWAT can be incorporated; this must be considered in advance. Trial and data management processes in the host study may need to be adapted to accommodate data collection for the SWAT, as well.

Deciding how and when to conduct randomization for a SWAT in a minimally disruptive way for the host trial is also vital, Ahmed et al. emphasize.

"Planning this carefully in advance will help to avoid confusion and minimize burden for participants, staff and researchers," they write. "It is likely that additional work will be required to embed the SWAT in a host trial and this may have financial as well as workload implications, so should be [factored into] funding applications."

There are other factors to consider as well. For example, some decentralized trials aimed at improving a single element of inclusion, such as race, have seen unintended consequences in other inclusivity elements, such as education and gender, the authors caution. Without systemic application of tools such as SWATs to provide concrete evidence of the actual effects seen with inclusion measures used, "researchers conducting decentralized trials may miss the opportunity to share outcomes and lessons learned in broadening participant inclusion," Noah Goodson et al. write in *NPJ Digital Medicine*.[5]

Efforts to increase SWAT-generated data about clinical trial operations are underway.

One such effort is the Promoting the Use of Studies Within a Trial (PROMETHEUS) program, which focuses on using SWATs to evaluate recruitment or retention strategies. The PROMETHEUS program was conducted between 2018 and 2021 and offered UK trial teams up to £5,000 (about $6,000) to embed a SWAT in their host trial. The group also provides methodological support, Laura Clark et al. explain in *Research Methods in Medicine & Health Sciences*.[6]

Under this program, 12 clinical trial units (CTU) applied for PROMETHEUS funding and 42 SWATs were funded and embedded in 31 different host trials across 17 different areas of health research. To date, it's the biggest single effort to generate SWAT evidence worldwide. Most of the SWATs focused on participant enrollment, such as assessing changes to patient information sheets. Others evaluated methods for training staff responsible for recruiting participants, Clark et al. say.

Several key lessons on planning SWATs have emerged from the program, Adwoa Parker et al. note in their paper on the PROMETHEUS program in *Health and Social Care Delivery Research*, including the need to ensure that sponsors have clear, accessible information about the nature of SWATs embedded in their trials and their role in supporting them.[7]

Equally important is involving patient and public involvement partners (PPI) in SWAT research, Parker et al. write. This involvement should mirror the way PPIs are consulted and included in development of the main trial. PPIs can be especially useful in developing novel and untested recruitment and retention strategies and adapting existing strategies to a specific host trial and patient population.

Finally, continually updated research priorities must be readily available to allow researchers to address questions relevant at a given time during a clinical trial. When SWAT priorities are established, methodologists must provide enough information to let study teams make informed decisions when evaluating priorities. This must include clear and consistent communication of SWAT priorities to research site teams, Parker et al. said.

"As the evidence base develops for effective and cost-effective recruitment and retention strategies, it will become increasingly important for trial teams to use this evidence base to inform their recruitment and retention activities," Parker et al. write. "Trial teams need to actively engage with the evidence base to inform their practice. Funders will need to actively support the trials they fund to use evidence-informed recruitment and retention strategies."

Some clinical trials may have capacity to address more than one SWAT question. This can be done separately or simultaneously using a factorial design, Parker et al. add.

## How to use SWATs to evaluate recruitment and retention

There are a variety of questions that SWATs can be used to address in clinical trials. As shown in the PROMETHEUS program, they are especially well-suited for evaluating the recruitment and retention of clinical trial participants.

For example, one SWAT found that personalization of study invitation letters may increase recruitment rates, Joanne

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Woodford et al. write in *Contemporary Clinical Trials Communications*. That SWAT was part of host trial ENGAGE, a feasibility study of an internet-administered, guided, cognitive behavioral therapy-based self-help intervention for parents of children previously treated for cancer.[8] The randomized controlled SWAT compared effectiveness of an invitation letter that included the potential participant's name and address vs. one that was not personalized.

"Even moderate effects of the personalization of study invitation letters on recruitment rates may be of significant value by shortening study length, saving resources and providing a faster answer to the clinical question posed by the study," they write.

In another approach, Christopher Dwyer et al. describe a SWAT protocol that compares the recruitment and retention efficacy of patient-designed participant information sheets vs. standard information sheets designed by researchers.[9] In addition to participant recruitment and retention figures, the protocol measures decision certainty, understanding of the information provided and likeability of the sheet, according to the *HRB Open Research* paper.

This SWAT is embedded in a trial of a program intended to improve cognitive and daily functioning for people with multiple sclerosis (MS). During the study, 120 people with MS will be randomly put in two groups for the double-blind SWAT, one receiving the standard sheet and the other getting the patient-designed sheet.

The standard information sheet, written by a researcher with more than 10 years of research experience, largely follows information sheet templates from past trials. It includes information on the study background, procedures, participant eligibility requirements, consent, descriptions of potential risks and benefits, and information on funding and support for the study.

The patient-designed sheet, developed by a PPI member of the research team, includes both necessary information that is specific to the trial and information that participants may find helpful. A PPI focus group reviewed and approved the latter.

In another *HRB Open Research* article, Sinead Duane et al. describe a SWAT to evaluate the recruitment and retention impact of a digital multimedia presentation on a handheld device vs. a standard written patient information sheet and both methods at once.[10] The SWAT aimed to measure whether recruitment and retention are increased with the digital option and how use of the tablet affects the quality of participants' decision-making.

The SWAT was developed for embedding in a clinical trial involving urinary tract infection (UTI) treatments. But Duane et al. note that the host trial was stopped before any participants were recruited due to emergence of new evidence on UTI treatments, so the SWAT was never implemented. However, they say lessons learned while developing the protocol could still "offer guidance to researchers who wish to answer similar research questions in the future in a similar context or setting."

"Understanding how to maximize the recruitment process will help to overcome challenges in the future and would benefit trialists during the design and implementation phases of trials," they write. "Developing and evaluating interventions aimed at improving recruitment to trials may be a good investment, where even a small return could translate into avoidance of substantial additional costs whilst reducing the time to potential knowledge impact."

Treweek et al. write that SWATs could be used to:

- Compare the effect of different financial incentives to encourage patients to complete a questionnaire used to collect trial outcomes;
- Determine whether recruitment is boosted if nonresponders to postal invitations to join a trial are reminded by telephone;
- Evaluate the effect on recruitment and retention of a two-stage patient information leaflet delivered in both a short "key points" version and a longer version containing more detail compared with a standard, single-stage leaflet;
- Measure the effect on data quality of providing site staff with face-to-face data entry training compared with video conference training; and
- Explore which type of information participants think would best recognize the value of their contribution to the host trial results.

### How to use SWATs to measure other study processes

SWATs can be used to measure a number of critical study elements, including patient satisfaction, informed consent and patient-recorded outcomes.

#### Patient Satisfaction

Angelica De Nardi et al. discuss the patient satisfaction angle in a *Research Methods in Medicine & Health Sciences*

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paper on a SWAT that compared two ways of delivering individual results to older clinical trial participants.[11]

While important, communicating and disseminating individual results to clinical trial participants is an unusual practice, they note in the report on results from a SWAT embedded in a trial on hypertension approaches in the elderly (HAEL study). The SWAT investigated two delivery formats of individual results to older trial participants with an eye toward determining if the formats improved understanding and satisfaction, as well as what short-term psychological impact they had.

Delivery of individual results was conducted in either individual or group meetings at a research site. Outcomes from the SWAT were assessed via participant answers to a multiple-choice questionnaire. Questions were related to five variables: cholesterol, body mass index, functional tests battery, blood pressure and cardiorespiratory capacity. Participants were deemed to have "adequate understanding" when they answered four to five questions correctly. Fewer than four questions answered correctly were considered to show "inadequate understanding."

Participant satisfaction was gauged by responses to questions considering the object, quality and effect of delivery of the individual results, while psychological impact was assessed in terms of questions about the participants' level of concern, level of anxiety, fearful feelings and feelings of sadness.

Most participants showed a good understanding of their results using both individual and group meetings. Satisfaction with the delivery format was reported in both groups, with "moderate negative emotional impact," De Nardi et al. write.

### Informed consent

The informed consent process is a crucial part of enrollment. Marah Elfghi et al. describe in a recent *Trials* paper a SWAT to evaluate the impact of same-day consent vs. delayed consent on participation recruitment and retention in a host trial evaluating the effectiveness of an intensive lifestyle modification program in patients with peripheral arterial disease.[12] In the SWAT, potential participants were given the option to consent immediately, on the same day they were invited to take part in the study, or to delay their consent.

The SWAT showed significantly lower withdrawal of consent among the same-day consenters, Elfghi et al. report. There was also a lower dropout rate in participants following the same-day consent approach. Transport was the main reason mentioned for consent withdrawal and dropout.

Among participants randomized to the host trial's intervention arm, significantly more same-day consenters completed the 12-week program compared to participants who delayed consent, Elfghi et al. say.

In short, they write, "this SWAT found evidence that participants who gave consent on the same day seemed to have better adherence and fewer consent withdrawals and dropouts."

Some patient populations may have special needs that aren't met by standardized consenting procedures. For example, trials involving adults with impaired capacity to consent raise ethical and methodological challenges. As a result, this group is often excluded from trials, Victoria Shepherd et al. note in a recent article in *Trials*.[13] Some of these challenges include communicating with family members who act as proxy decision-makers.

"Family members are often given little information about their role as a consultee or legal representative," Shepherd et al. write. "Some family members find making a decision about trial participation difficult and may experience an emotional and decisional burden as a result. Families have reported a need for greater support and guidance when making such decisions."

Shepherd et al. report a prospective SWAT to evaluate how well a decision aid supports such family members in making more informed decisions about clinical trial participation. The decision aid has undergone acceptability testing both with researchers who would deliver it and representatives of patient families who would receive it.

The aid will be initially embedded in a single host trial, but the plan is to include it in approximately five studies that recruit adults lacking the capacity to consent.

### Patient-recorded outcomes

Patient-reported outcomes (PRO) are another area in which different approaches may yield different results. Lara Philipps et al. describe in a recent *BMJ Open* article a SWAT on electronic vs. paper-based patient-reported outcomes collection (SPRUCE) to evaluate the acceptability of ePRO in oncology clinical trials.[14]

At the Clinical Trials and Statistics Unit of the Institute of Cancer Research (ICR-CTSU), PROs are collected using paper questionnaires. The SWAT aims to compare the SPRUCE PROs, developed with input from patients and public contributors, to those paper PROs. The ePRO comparison can

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run in multiple host trials with a partially randomized patient preference design that lets trial participants choose to be randomized or to choose their PRO preference.

The primary objective will assess differences in return rates or compliance between ePRO and paper PROs in the randomized group, Philipps et al. explain. The SWAT aims to assess acceptability of ePRO in oncology clinical trials, establish whether ePRO is acceptable to ICR-CTSU trial participants and determine whether it can capture complete PRO data on par with paper PROs.

### Emerging uses for SWATs go beyond process evaluation

Although there is limited evidence of SWATs evaluating trial processes other than recruitment and retention strategies, Ahmed et al. note, SWATs can allow evaluation of other trial aspects as well, including participant engagement or compliance with treatment plans.

They present two case studies of SWATs testing the use of video animations to improve intervention implementation, focusing on enhancing participant understanding, including uptake, engagement and compliance. Uptake is defined as the participant proceeding with the intervention following the initial visit from a treatment provider. Engagement refers to the participant's understanding and responsiveness to the treatment. And finally, compliance refers to the extent to which the patient accepts the treatment at the frequency and duration specified.

Both SWATs are embedded in randomized trials and test a similar intervention. But the host trials differ in aspects of design, intervention, setting and population; the SWATs themselves have different rationales, randomization and outcomes.

The first case study involves a SWAT embedded in a clinical trial evaluating whether personalized care planning for frail older adults improves quality of life and reduces health and social care resource use. The SWAT aims to determine if video animation used to introduce the planning improves participants' uptake and engagement with the intervention, measured by how many participants receiving the video animation attend the first intervention.

The second SWAT evaluated whether a service-level intervention for stroke survivors targeting reduction of sedentary behavior improves extended activities of daily living and cost-effectiveness. The SWAT aimed to test whether video animation added to the trial intervention increased participant understanding, engagement and intervention compliance and whether it reduced sedentary behavior.

"These are important aspects of intervention implementation as they are directly linked to intervention effectiveness and therefore important to study," Ahmed et al. write. "We have proposed that it is possible to embed SWATs to investigate and refine a relatively unexplored area of trial conduct, namely intervention implementation processes. If the refinements are shown to enhance intervention implementation, they could be used as evidence-based strategies to facilitate implementation of complex interventions in future trials."

SWATs such as these could be especially useful during the feasibility state of clinical trial development, when more refinement of an intervention is possible, they add.

Beatriz Goulau et al. present a case study in a recent issue of *Trials* in which a re-randomization design is used in a SWAT to test whether adding a sticker with the trial logo to the envelope in which questionnaires are sent to patients would result in a higher response rate compared to envelopes without a sticker.[15]

They note that the randomization design is an important factor in ensuring an adequate sample size. This design would allow trial participants to be re-enrolled and re-randomized whenever a new retention opportunity occurs. At such points, the SWAT intervention could be reapplied because a new questionnaire or clinical appointment to collect data is taking place, they explain.

Re-randomization designs have been used to evaluate treatments for clinical conditions where some trial participants may require treatment on more than one occasion, Goulau et al. write. Examples include sickle cell pain crises, severe asthma exacerbations, flu vaccines, in vitro fertilization and preterm birth. In these cases, study participants were re-randomized for each crisis or event.

A similar approach could be used for SWATs evaluating interventions that could be used more than once, they suggest. For example, an alternative retention intervention could include a text message reminder for each new questionnaire issued to study participants. Patients could be re-randomized for each text reminder.

"By allowing participants to be re-enrolled at each new data collection point, re-randomization designs provide larger sample sizes than parallel group trials and estimate the effect of the intervention each time it is used, rather than only the first time," they write.

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There are other advantages, too, Goulau et al. add:

- It would allow estimation of an average effect over time, increasing generalizability;
- It could be more efficient than a parallel arm trial due to increased sample size; and
- It could allow subgroup analyses to estimate effectiveness at different points in time.

### How SWATs can monitor good clinical practices

Monitoring methods offer another opportunity for SWATs to help gauge the relative effectiveness of different approaches, according to Katherina Klatte et al.[16]

Klatte et al. searched a variety of sources — such as CENTRAL, PubMed and Embase — for relevant published literature up to March 2021. They also searched the online SWAT repository and trial registries for ongoing or unpublished studies.

"Trial monitoring is an important component of good clinical practice to ensure the safety and rights of study participants, confidentiality of personal information and quality of data," they write. "However, the effectiveness of various existing monitoring approaches is unclear."

Klatte et al. identified five monitoring strategies that could be compared in a SWAT model:

- Risk-based monitoring based on an initial assessment of the risk associated with an individual trial protocol;
- Central monitoring with on-site visits triggered by schedules based on initial risk assessments at different sites;
- Central and local monitoring, based primarily on central monitoring along with local quality control by qualified personnel on-site;
- Monitoring with targeted or remote source data verification, where only regulatory and scientific key data are verified; and
- On-site initiation visits upon request, where systematic visits are replaced by visits that take place only upon investigators' requests at a site.

"The evidence base is limited in terms of quantity and quality," they write. "Ideally, for each of the five identified comparisons, more prospective comparative monitoring studies nested in clinical trials and measuring effects on all outcomes specified in this review are necessary to draw more reliable conclusions."

## The financial benefits of clinical trial SWATs

The cost of clinical trial operations is a continual source of concern for sponsors, CROs and research sites alike. SWATs can offer an opportunity to evaluate whether alternative approaches to certain processes can add or reduce the expense associated with a trial or type of trial.

For instance, Mbathio Dieng et al. describe in a *BMJ Open* article SWAT evaluation of the incremental costs of a psychoeducational intervention for clinical trial participants with a history of melanoma.[17] Psychological support programs are not currently funded for this group of patients, they note, largely due to lack of cost-effectiveness data. The cost-focused SWAT will be embedded in a trial studying the health outcomes of such support within the Australian healthcare system.

The SWAT will include cost-effectiveness and cost-utility analyses, Dieng et al. write. Costs associated with the development of the psychoeducational intervention include development and pilot testing of a booklet entitled *Melanoma: Questions and Answers*, along with development of an intervention manual, psychologist recruitment and training, and pilot testing of the intervention. Human resource records and intervention development team records will be used for the valuation of these costs, they explain.

Trial-associated costs will consider salaries of involved study staff, psychologist salaries, administrative costs of coordinating the SWAT, production of the SWAT materials, postage, weekly clinical supervision costs and telephone use.

Not included is the cost of the Cancer Council booklet *Understanding Melanoma*, which is routinely offered in melanoma clinical trials. That booklet will be provided to both participants receiving the additional psychoeducational support and those that do not, so its cost is identical in both groups.

## The challenges of SWAT implementation

SWATs can add immeasurable value to the clinical trial process by providing concrete evidence of the benefits — or lack thereof — associated with a change in procedure. However, since the dataset of evidence generated from SWATs remains scant, caution is warranted when attempting to apply information gleaned from a SWAT.

"Mistargeting an improvement intervention for a single trial may result in wasted resources, but when developing generalizable interventions for trial improvement, this mistargeting may bias the estimates of trial improvement efficacy towards the null, inappropriately suggesting interventions are

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ineffective when really they just are not addressing the right problems," Stensland et al. say.

For example, a SWAT where host trial sites are randomized to receive supplemental research staff or standard staffing, aiming to increase trial enrollment, may show no benefit to hiring additional staff. But this could be because some sites have already reached full penetration of eligible trial participants. If the SWAT included only sites with low adoption, especially if due to lack of resources at those sites, more trial staff could prove to be beneficial. If contextual elements are not assessed, the SWAT findings have only limited transferability.

"By specifying the characteristics of trial sites and 'diagnosing' determinants of trial success, we can design and evaluate trial improvement interventions for various contexts to maximize value," Stensland et al. write.

Another challenge could lie in how well-prepared a site is to implement SWATs as part of their overall clinical trial operation. Some sites may not engage as well with SWATs as others, Clark et al. note. According to data gleaned from the PROMETHEUS program, the reasons for this can include workload and prioritization issues. Sites with busy trial portfolios may find it hard to make the time to address the SWAT objectives, despite their best intentions. And there may be insufficient or no incentives for a team to embed a SWAT within their host trial, the authors add.

Meanwhile, some researchers may not find the SWAT questions as interesting or engaging as those for the host trial. If a PI expresses such an opinion, this can drive interest away from a potential SWAT, Clark et al. write.

"For instance, although each SWAT should produce a peer reviewed paper in terms of contributing to a Research Excellence Framework it is unlikely any individual SWAT publication will form part of an institution's submission," they write. "Uplift of the importance of SWATs is necessary to avoid this in the future, with senior institutional management needing to fully engage with SWAT programs."

And some organizations may struggle to determine which SWAT is a good fit for the host trial's target population, design or processes, Clark et al. say. Identifying effective ways to communicate which SWATs — including recruitment, retention and other methodological interventions — are the best fit for specific trial characteristics can help with this issue. An additional approach could be creation of a clear list of SWAT research priorities, including both SWAT details and trial areas, that sponsors and researchers can both reference.

## Seven key factors that affect SWAT implementation

Many of those challenges can be overcome through careful consideration of seven practical considerations that Treweek et al. say must come into play whenever a SWAT is considered for any clinical trial.

### 1. Cost

At the top of the list is cost. The high cost of research waste means the SWAT cost considerations are critically important, Parker et al. write. For this reason, trial teams should conduct streamlined economic evaluations alongside future SWATs, they suggested. This can include the cost per additional patient recruited or retained.

Additionally, the value of information analyses can help determine whether or not further SWAT evidence is beneficial in areas where several SWATs already exist.

A real-time, dynamic communication strategy, including cost and resource breakdowns, should be developed for each suggested SWAT, Parker et al. write. This will ease the burden of costing exercises on trial teams and help speed an informed decision about whether it's feasible to embed a particular SWAT into a clinical trial.

"Pragmatic decisions on which SWAT may be appropriate and feasible to include should be taken as required," they write. "A mechanism to communicate SWAT research priorities is needed and this information needs to be readily accessible for all trialists to refer to."

Treweek et al. purport that SWATs don't have to be particularly expensive; they may range between $6,000 and $12,000 based on past experience.

"Ideally, they should be built into the host trial from the start and the associated costs can be included in the budget for the host trial," they write. "If the findings of the SWAT will be reported in a standalone publication in an author-pays open-access journal, the costs of this will need to be budgeted for."

### 2. Randomization

Randomization is the second key consideration when inserting a SWAT into a clinical trial, according to Treweek et al. Some SWATs may not require randomization. For example, if a SWAT is meant to evaluate the effect of alternative ways of doing a trial process, the options being compared should be allocated at random. On the other hand, if the goal is to understand why something is done the way it is, randomization is likely to be inappropriate and other qualitative methods would be required, Treweek et al. say.

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When it is required, SWAT randomization can be done separately from the host trial's randomization process.

### 3. Ethics

The third consideration for SWATs is ethics. Treweek et al. note that ethical approval guidelines and regulations for clinical research vary among countries. Depending on the specific SWAT protocol being evaluated, specific national rules may require ethical approval with an IRB or similar review panel. For example, it is likely that any SWAT within a host trial in the EU will require approval under Directive 2001/20/EC of the European Parliament, they write.

For trials not governed by the directive, national requirements can vary widely. For instance, in the UK, SWATs that involve National Health Service patients will likely require institutional review and ethical approval. In the Republic of Ireland, ethical approval usually would be sought from sites conducting the host trial and/or from the SWAT PI's host institution.

However, if a SWAT is planned at the same time as the host study, it could be included in the application for ethical approval of the host trial.

### 4. Informed consent

The importance of informed consent varies among different trials and different participant populations.

"SWATs are generally low risk and it is rare for them to impose additional burden or risk on participants [so] it will not usually be necessary to get individual consent from participants," Treweek et al. write. "Indeed, in many cases individual consent may not be appropriate. It may confuse patients as to what they are consenting to and may impact their behavior if they are aware that different recruitment methods are being tested, confounding the evaluation."

### 5. Data analysis

Another consideration is how the analysis of SWATs will be carried out. This analysis might be simple, such as comparing two proportions, Treweek et al. say; it may be done by members of the trial team other than a senior statistician.

Sample size calculations for SWATs can be done by using estimates of minimum important differences that investigators or others deem appropriate. The size of the SWAT is constrained by the host trial, Treweek et al. note. The size of a recruitment SWAT, for example, may be larger than the host trial sample size. The constraint is the size of the patient population vs. the number of trial participants. Other SWATs, such as those focused on patient retention, will be limited to the actual host trial sample.

However, they point out, "it is highly unlikely that the size of the host trial will be changed for the benefit of a SWAT. SWATs are designed for future meta-analysis. In other words, while an individual SWAT may be underpowered, a meta-analysis of several well-done SWATs evaluating the same intervention and following the same protocol can provide compelling evidence for trial process decision making."

SWATs exploring qualitative questions about how a trial process is delivered, organized or perceived should be analyzed via a suitable qualitative method, they add.

### 6. SWAT design

Trial teams also must consider exactly how a SWAT will be implemented. Some SWATs may require extra work, such as putting additional materials, incentives or information leaflets into envelopes for trial participants. This work may be done by temporary staff or full-time employees who have a lull in their trial-related work. Other SWAT-related work could include using mail merge software to generate different invitation letters for study participants.

One issue to consider when assigning these tasks is whether confidentiality or data protection requirements may limit who can do this sort of work, Treweek et al. say. If the potential exists for identifying participants to individuals who would not otherwise have lawful access to personal identifiable information, for example, only authorized study personnel can perform these tasks for a SWAT.

### 7. SWAT reporting

Finally, the findings of any SWAT should be accessible in the public domain. This might be accomplished through inclusion in host trial reporting, with appropriate signposting — possibly in the abstract — to highlight its presence, Treweek et al. write. Other options include a standalone dedicated publication addressing the SWAT results or inclusion in a relevant systematic review.

Parker et al. note that reporting guidance is needed, as well, to ensure that publications include sufficient information to evaluate SWATs.

With all these factors considered, carefully developed SWATs can provide a valuable resource for research teams and organizations. By using randomization and controlling the data generated, these studies can provide robust feedback

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about the true value of various critical clinical trial processes.

While site-specific challenges must be considered, Parker et al. recommend that PIs and other research team leaders consider embedding SWATs in clinical trials as early as possible, ideally at the funding stage.

"As the evidence base develops, it will become increasingly important for trialists to utilize the evidence base in a systematic way to identify both effective and ineffective strategies to inform their practice," Parker et al. write. "Future work should therefore consider issues around the dissemination and implementation of SWATs and develop guidance to enable the wider trials community to undertake, report and adopt the findings of SWATs. Implementation science, the study of methods to promote the uptake of evidence-based practice, could be used to inform any such future work."

It is likely that heavy focus will remain on recruitment and retention SWATs, as well as those in related areas such as patient satisfaction and informed consent. But current publications indicate that there are myriad additional ways in which SWATs can and should be utilized to boost the efficiency, effectiveness and quality of clinical trial operations.

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Ideally, CRAs are trained to evaluate all clinical research investigators, study coordinators and other staff equitably. Unfortunately, this is not always the case. And even well-trained CRAs can't simply intuit a new hire's ability to do their job. It's up to research sites to provide supporting evidence of their qualifications.

### Don't assume 'new' employees are inexperienced

The term "new" does not fit a single definition or category. Investigational research sites are as diverse as the personnel they employ and require unique and specific consideration during the site evaluation visit relative to the site model, personnel and training practices to discover the extent of their capabilities.

Most investigational sites have new or inexperienced staff. It is a standard part of site operations with personnel retiring, leaving and the need to fill vacant positions with available candidates. There is no set clinical research standard to quantify sufficient experience, such as a specific number of years in the field or a number of completed trials.

Experience is relative. In the clinical research industry, it is generally accepted that if a coordinator has a year or more of coordinator experience, they are not lacking experience. With PIs, quantifying experience can be a bit more complex; the number of trials conducted and time in the role both count. A newer PI may have participated in 10 studies in less than a year due to site models and workloads, while an academic PI may have participated in only three studies over two years due to the nature of academic models.

A new coordinator may have experience in other roles, such as recruiting or data management. A new PI may have worked as a support investigator during a clinical fellowship. Neither one is truly new to clinical research. Likewise, if a clinical researcher is truly brand-new to both clinical research and their role, they may have alternative medical or health training that could supplement that missing clinical research experience and provide a solid foundation of understanding to expedite the learning process.

This nuanced information can be demonstrated during an evaluation visit with information that presents a holistic view. For example, a new PI who has extensive therapeutic experience from years spent in a specialty clinical practice, such as endocrinology, pulmonology or cardiology. Clinical research and clinical practice in that specific therapeutic area have shared procedures, diagnostics and treatments that help bridge the learning gap and more easily transition to the PI role.

And a coordinator may have extensive experience as an oncology or trauma nurse with transferable therapeutic area skills even if they still need training in the clinical research process. That should be less difficult for someone with this advanced clinical background. A new coordinator who is also an experienced trauma nurse could almost immediately support some duties on a trauma/shock clinical trial, for example.

Sites must share this information with CRAs to help them conduct an equitable evaluation.

The study sponsor is responsible for selecting investigators and institutions, according to the International Conference on Harmonisation (ICH) good clinical practice (GCP) guideline ICH E6.[1]

"Each investigator should be qualified by training and experience and should have adequate resources to properly conduct the trial for which the investigator is selected," the guideline notes.

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The words "training" and "experience" from ICH E6 do not mean that all inexperienced or new clinical researchers are not qualified, however. The regulations are very broad, according to the FDA's Good Clinical Practice Program (GCPP).[2] "Training, education and experience required for sponsor personnel may necessarily and appropriately vary depending on the type of product, the indication, the study being conducted and its associated risk," is GCPP's stock answer to questions about training requirements.

Investigational site identification and evaluation is not an automated process with a yes-or-no checklist. The process answers a variety of questions, starting with the preliminary feasibility questionnaire through to the formal prestudy evaluation visit checklist to fully characterize the investigational site model and staff capabilities. It should include sections for aligned therapeutic expertise, access to the patient population and questions about equipment, facilities and personnel.

But feasibility questionnaires do not always have targeted questions to identify lack of experience or related and relevant experience. Some better designed questionnaires include questions about therapeutic expertise and patient access with subsets of questions about clinical trials conducted in the specific therapeutic area that allows the site to detail clinical research, therapeutic experience or both. Sires should ask about these.

"FDA's regulations are not explicit as to what constitutes adequate training, education and experience, nor do they outline specific qualifications," GCPP notes. "The sponsor has discretion to determine what qualifications are needed in certain positions based on the general recognition that this would include education, training and experience pertinent to the particular clinical study and its design and execution, as well as familiarity with human subject protection regulations, recordkeeping, data integrity and [GCP] standards and requirements."

A lack of investigator or coordinator experience should not be the prohibitive factor in site selection of an otherwise capable and competent site.

Unfortunately for industry, it sometimes is. The most qualified potential investigational site partner may run the risk of not being selected for the study if they propose an inexperienced PI or coordinator. Some sponsors are simply reluctant to use sites with new investigators or study coordinators at the helm.

What matters most and what can mitigate these concerns are the investigational site training standards and processes to ensure new research staff understand clinical research regulations and study activities and that they are supported by experienced mentors and colleagues throughout the learning process.

## Be transparent when communicating capabilities

Transparency and trust are integral to building sponsor/site relationships in the study startup phase. Site evaluation is a reciprocal consideration between the investigational site and sponsor; transparent measures and trustworthy information are required by both in order to make an informed decision about site participation. Investigational sites are obligated to inform potential sponsors if their proposed PI or coordinator is new to their role, just as the sponsor selecting investigational sites must be forthright about any reservations they have moving forward with inexperienced PIs or coordinators during the site evaluation process. To build lasting partnerships, the data from both sides must be reliable.

The investigational site should ensure they have completed or are working on all required clinical research and role-specific training and can speak to these preparation measures during the site evaluation visit. They should also be able to discuss their alternative clinical and clinical research experience to address concerns or supplement perceived deficiencies.

For example, the site should:

- Disclose whether site leaders need additional training to supplement and to complete the trial (i.e., GCP training);
- Show team members' desire and willingness to complete the additional training and protocol requirements in a timely manner;
- Provide information about backup personnel, whether or not they have research experience and the type of and quantity of that experience;
- Confirm that the study leaders have reviewed the study information provided prior to the visit and have a desire to complete the trial responsibilities; and
- Confirm the PI and coordinator have time to complete study requirements, including meeting with and talking to the site monitors onsite or using remote technology.

## Delve deeper to ensure equitable decisions

The answers to these questions are pivotal in demonstrating the adequacy and desire of inexperienced staff. But there are additional points site evaluators might discuss with investigational site staff during the visit to ensure an equitable and informed decision. Sites should anticipate and prepare for these.

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For example, the CRA will look to determine the breadth of the PI's or coordinator's clinical and research experience. If a PI proposed by an investigational site is new to their role, the CRA should delve deeper to determine all of their investigator experience.

Sites should also prepare to answer questions about staff members' specific experience in a research support role or participation in clinical trials during residency or fellowship. In fact, some support investigators can have more procedural or patient care research experience than their PI counterparts serving in an oversight position with little exposure to participants during trial visits. An experienced support investigator can successfully transition to the role of PI as they already possess a strong understanding of the responsibilities.

During residency/fellowship training the investigator may have supported research activities by completing physical exams, reviewing medical records for eligible study patients or drawing/processing study labs. Research experience in any capacity is still genuinely transferable towards overall understanding of clinical trial responsibilities.

Sites can also highlight the experience as a medical assistant or nurse to show staff are well-versed in medical procedures, such as recording vital signs, conducting electrocardiograms and phlebotomy or medication preparation and administration. Data entry, recruitment or regulatory activities are also valuable and can be missed during the interview because they are not "direct" experience.

Sites must be able to communicate that any research experience is valuable research experience that contributes to the assimilation process and be prepared to share transferable clinical and research skills with the CRA.

The CRA may also ask whether proposed personnel have guidance from and oversight by an experienced colleague. The new PI should have an experienced researcher assisting them or have access to an experienced investigator who can mentor them. This is especially important during critical periods of screening and enrollment, recording serious adverse events (SAE) and conducting informed consent and protocol deviations. This additional level of oversight will help ensure accuracy of data and adherence to study procedures. It also shows the site's due diligence in new staff training/development.

Sites should assure the CRA that there is an experienced person to serve as the backup or provide guidance for that specific role. Another option is to use an experienced coordinator as the primary coordinator, with the new coordinator serving as the backup for several months until the candidate gains additional experience. A role change may require additional administrative paperwork, but it will provide the coordinator the critical experience needed to eventually assume the role of PI.

The CRA might also ask about the level of institutional leadership involvement. There are potential risks when an investigational site or department consists of primarily inexperienced research staff and lacks experienced research leadership. For example, a research organization may have a department head who is also an experienced physician investigator and will oversee a new PI or coordinator and set training and onboarding policies for new staff. At the dedicated research site or private practice, the new PI or coordinator may be supported by an experienced site director and/or other investigators who can directly observe training and ensure compliance. When inexperienced staff are directed by experienced leadership willing to make an investment in training and guidance, it makes the assimilation of the new role and responsibilities that much more effective.

## Use training programs to prepare new personnel

The research organization must also be able to describe the extent and type of training completed by the candidates to prepare them for their respective roles. A savvy research institution proposing a new PI or coordinator to potential sponsor partners will ensure they have completed a comprehensive list of training as part of their onboarding to elicit sponsor trust and to demonstrate their commitment to quality. The key to setting up new PIs for success is to "correctly train new-to-research sites the right way from the very beginning to provide quality data," Lisa Dyment, senior director of site collaborations at PPD, and her colleagues write in *PharmaFocus Asia*.[3]

"Effective training drives repeat participation by physicians and healthcare providers in clinical trials by equipping them with the knowledge, skills and desire to perform successfully."

Robust training programs develop and upskill workforce capabilities across the clinical research industry, improve sites' ability to deliver quality outputs, promote career expansion and development "and bring clinical trials closer to the patients who need them," Dyment et al write.

There are many important areas of training focus for new PIs and coordinators, among them:

- IRB process;
- Investigator responsibilities;
- GCP and human subjects protection principles;
- SAEs/AEs and safety reporting;

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- Investigational product control;
- Informed consent; and
- Protocol content.

They also must be taught the difference between clinical research and clinical practice, the role of the investigator, the role of the study coordinator, study phases and federal regulations. Among the FDA's clinical research guidance documents are some specific categories from which new investigators and coordinators would benefit, including:

- Informed consent guidelines;
- Exceptions to informed consent requirements for emergency research;
- Recruiting study subjects;
- Participant payment and reimbursement;
- Centralized IRB review process in multicenter clinical trials;
- Oversight of clinical investigations and risk-based monitoring;
- Clinical investigator financial disclosures;
- Safety reporting requirements for studies; and
- Electronic informed consent.

There are training programs available through the National Institutes of Health, the Association of Clinical Research Professionals (ACRP) and other organizations. Institutional research SOPs and onboarding procedures should all be completed and documented. The CV should reflect all training completed.

Institutional policies and resources determine the training method. Larger and more established sites may use formal learning and practice-training workshops, outsourced group training and online learning programs.

For practical coordinator training, some investigational sites have an observation and evaluation process, also known as "see one, do one" learning. In this model, the new coordinator observes an experienced coordinator completing a research process, such as informed consent, study drug administration, vital signs, specimen processing, patient recruitment, and study visit scheduling and documentation. Then the experienced coordinator would observe and confirm the new coordinators' competency in independently completing the same tasks.

The investigational site may consider providing training details of new proposed staff to the CRA during the site evaluation visit to lend credence and reassurance. All training activities should be well documented and verified by the CRA during site evaluation.

There are also benefits to certification for new investigators and CRAs should confirm these. "It is important to get certified in clinical trials, as certification allows investigators new to clinical research to maintain regulatory and ethical compliance and deliver quality clinical trial outcomes," writes Moe Alsumidaie, head of research at ClinBiz, a consultancy, in *Applied Clinical Trials*.[4]

ACRP and the Society of Clinical Research Associates, as well as some universities, offer certification for investigators and coordinators.

When preparing for an evaluation visit, sites should ensure all personnel, including PIs, coordinators and research assistants, are responsive and attentive during the process. Encourage new staff, especially, to demonstrate enthusiasm and interest to prospective sponsor partners. All must be apprised and consistently aware of study directives, status and current information. Demonstrating familiarity with the protocol and asking insightful questions and preparing information that supports selection will lend credibility.

All of this preparatory work can be completed through formal research team meetings at specific intervals or one-on-one informal conversations with specific team members. The PI should also meet individually with the assisting investigators to discuss the patients who will be treated and other important clinical information. The coordinator should meet with the site director or alternate coordinator consistently as part of an onboarding training program. The key to staying on top of study responsibilities, especially when new, is through information-sharing.

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# Exam for Continuing Education

## Research Practitioner, Vol. 24, No. 06, 3.0 Contact Hours

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### SWATS

1. What is the purpose of a study within a trial (SWAT)?
   a. To evaluate the scientific integrity of a clinical trial.
   b. To evaluate approaches to trial processes.
   c. To generate evidence on the efficacy of clinical trials.
   d. To measure patient satisfaction in a clinical trial.

2. Which of the following best describes a key feature of a SWAT?
   a. It impacts the scientific integrity and outcome measures of the host study.
   b. It is only suitable for a single clinical trial and cannot run across multiple trials.
   c. It has its own protocol and is embedded within a host trial.
   d. It is designed to maintain uncertainties about trial processes.

3. Which of the following best describes evidence that researchers can glean from SWATs?
   a. The safety and efficacy of clinical trials.
   b. The efficiency of clinical trial operations.
   c. The long-term implications of financial incentives on recruitment.
   d. The importance of patient satisfaction in trials.

4. Which of the following describes something researchers can evaluate using a SWAT?
   a. Site locations.
   b. Informed consent.
   c. Drug safety.
   d. Data quality.

5. Which of the following statements about SWATs is true?
   a. They affect the scientific integrity of the host study.
   b. They are designed to resolve outcome uncertainties.
   c. They can only be evaluated in a single clinical trial.
   d. They provide data to inform the design of future trials.

6. What is the main focus of the PROMETHEUS program?
   a. Investigating the impact of financial incentives on trial outcomes.
   b. Assessing patient satisfaction with individual result delivery methods.
   c. Evaluating different strategies for participant recruitment and retention.
   d. Measuring the effect of data entry training methods on data quality.

7. Which of the following best describes a finding from the PROMETHEUS program?
   a. Personalized study invitation letters increased recruitment rates.
   b. AI-generated participant information sheets improved patient satisfaction.
   c. Digital multimedia presentations had no impact on data quality.
   d. Decentralized trials had unintended consequences for inclusion.

8. Which of the following actions is most vital when conducting a SWAT?
   a. Deciding on the optimum trial duration for the SWAT.
   b. Avoiding contaminating SWAT data with host data.
   c. Randomization with minimal disruption to the host trial.
   d. Publishing scientific papers about the SWAT findings.

9. How can SWAT-generated data benefit future trials?
   a. By improving patient satisfaction in clinical trials.
   b. By eliminating the time required for recruitment and retention.
   c. By reducing costs and conserving resources.
   d. By ensuring scientific integrity and ethical practices.

10. Which of the following best describes a benefit of involving public partners in SWAT research?
    a. They provide valuable insights into novel trial process strategies.
    b. They are an inexpensive way to supplement trial staff.
    c. They help recruit participants from specific demographics.
    d. They disregard existing evidence-based recruitment strategies.

## Site Evaluations

11. During site evaluations, which aspect is crucial for making a good impression, especially concerning new research staff?
    a. The demographics of the new staff.
    b. The number of trials they have completed.
    c. How prepared they are for the visit.
    d. What medical equipment training they have.

12. How can research sites evaluate the preparedness of new research personnel?
    a. By conducting interviews with principal investigators and study coordinators.
    b. By assessing their experience and workload.
    c. By reviewing training policies.
    d. All of the above.

13. Which of the following are important when building a relationship between sponsors and investigational sites during the startup phase of a trial?
    a. Transparency and trust.
    b. Budgets and finances.
    c. Expedited regulatory approvals.
    d. Participant enrollment strategies.

14. Which of the following strategies can help mitigate concerns about inexperienced personnel during site evaluations?
    a. Revealing minimal information about staff.
    b. Focusing on strong theoretical training.
    c. Demonstrating alternative experience.
    d. Demonstrating strong social skills.

15. True or false: Not all research experience is valuable and relevant to the assimilation process.
    a. True.
    b. False.

16. Which of the following best describes a benefit to new team members of guidance and oversight from experienced colleagues?
    a. It allows them to work remotely.
    b. It helps them with administrative tasks.
    c. It ensures they adhere to study protocol.
    d. It ensures greater patient retention.

17. Which of the following tactics can help ameliorate concerns about new and inexperienced employees during a site evaluation?
    a. Propose a temporary coordinator with more experience.
    b. Assign more duties and tasks to the inexperienced coordinator.
    c. Prohibit them from performing critical tasks and direct patient care.
    d. Make their employment status conditional upon site selection.

18. Which of the following is a benefit of recruiting experienced researchers to mentor inexperienced staff?
    a. Reduced protocol deviations.
    b. Improved participant engagement.
    c. Risk mitigation and effective training.
    d. Decreased staff turnover.

19. Which of the following is a key element when preparing new PIs and coordinators for success?
    a. Focusing on specialized clinical trials.
    b. Access to in-depth training programs.
    c. Access to potential trial participants.
    d. All of the above.

20. What is the primary aim of robust training programs for new clinical research personnel?
    a. Cost reduction in clinical trials.
    b. Streamlining regulatory processes.
    c. Enhancing patient recruitment strategies.
    d. Equipping them with necessary knowledge.