CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

# STRENGTHENING THE INVESTIGATOR SITE COMMUNITY PROJECT

## Multi-Stakeholder Meeting

April 5, 2017

Sheraton Silver Spring Hotel
8777 Georgia Avenue
Silver Spring, MD 20910

CTTI MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials

## MEETING BACKGROUND

The US clinical research enterprise depends on an adequate supply of experienced, productive site investigators to conduct clinical trials that ultimately provide the scientific evidence needed to obtain marketing approval for new therapies. However, both anecdotal accounts and more systematic, evidence-based examinations suggest that the pool of qualified investigators has been shrinking in recent years and that a growing proportion of investigators stop leading clinical trials following a single experience conducting an FDA-regulated drug trial. The loss of knowledgeable and experienced investigators has worrisome implications for clinical research and could threaten the quality and efficiency of clinical trial conduct. A number of possible reasons for these increasing rates of investigator attrition have been advanced, including workload issues and logistical, financial, and regulatory burdens, but to date these potential explanations have not been thoroughly explored and characterized. CTTI's "Strengthening the Investigator Site Community" ("Investigator Community") project was undertaken to better understand why clinical investigators choose to remain engaged in clinical research practice or leave it after a single experience, and to develop strategies for strengthening investigator retention and reducing turnover.

## MEETING OBJECTIVES

- Present findings from CTTI's Strengthening the Investigator Site Community Project: Expert Interviews and Survey
- Receive feedback on identified challenges experienced by principal investigators and strategies to overcome these challenges
- Identify essential elements necessary to strengthen and grow the community of productive, experienced site investigators
- Develop strategies and best practices to promote the growth and strengthening of the community of experienced site investigators
- Identify barriers to strategy implementation and propose solutions

## MEETING EXECUTIVE SUMMARY

CTTI's "Strengthening the Investigator Site Community" project (referred to hereafter as the "Investigator Community" project) convened an expert meeting to address the problem of investigator turnover and retention in the US clinical trials enterprise. Participants included representatives from academic medical centers, private practice, industry (including pharmaceutical, medical device, and contract research organizations), government (including the National Institutes of Health and the US Food and Drug Administration [FDA]), and patient representatives.

Meeting participants shared findings from several studies designed to better characterize the phenomenon of investigator turnover and to develop a "phenotype" of investigators who withdraw from clinical research versus those who remain engaged in clinical trials over the longer term. There were also presentations from industry representatives who provided

background information about how sponsors and clinical research organizations (CROs) view issues related to the logistics and finances of clinical trials, and presentations from FDA representatives about training resources available for investigators and characteristics associated with success, or lack thereof, in conducting FDA-regulated trials.

Over the course of open discussion that took place at intervals throughout the meeting, a number of key themes emerged:

1. Clinical investigators and their study staff often have interest in and enthusiasm for conducting clinical research, but need access to training, mentoring, and supportive infrastructure (and in some cases, institutional support) to flourish as effective research sites.
2. Educational and infrastructural elements are not equally available across all clinical sites, with larger academic sites and large practices enjoying advantages relative to smaller practices, who sometimes struggle to establish themselves with research sponsors and CROs. In addition, specific training in site-based research is lacking among national training curricula.
3. Expanded access to education, training, mentorship, and supportive resources for investigators and staff are needed across the spectrum of research, but especially so for smaller practices and individual researchers who lack access to academic center resources.
4. Increased communication, education, and transparency around issues such as contracting, budgeting decisions, and site recruitment could benefit investigators and improve interactions with sponsors and CROs, as well as improving site performance.
5. Incorporating input from all stakeholders, including patients and experienced study personnel, can improve the process of protocol development, thereby enhancing the overall trial experience and reducing delays in study startup.

The Investigator Community project team will continue to review evidence gathered and incorporate input and insights from the expert meeting as it develops project recommendations and other products for dissemination.

# MEETING SUMMARY

## INTRODUCTION AND BACKGROUND

Matthew Roe (Duke Clinical Research Institute), Terri Hinkley (Association of Clinical Research Professionals), and Diana Foster (Society for Clinical Research Sites) welcomed the meeting participants and conducted roundtable introductions (a full list of attendees is provided in Appendix B).

### Introduction to the Clinical Trials Transformation Initiative (CTTI)

*Gerrit Hamre, Clinical Trials Transformation Initiative (CTTI)*


CTTI Project Manager Gerrit Hamre provided a brief overview of CTTI's background and mission. CTTI is a public-private partnership co-founded in 2007 by Duke University and the US FDA. Now with more than 80 member organizations, CTTI engages with a diverse group of stakeholders in conducting evidence-based, impactful efforts "to develop and drive adoption of practices that will increase the quality and efficiency of clinical trials."

### Issue, Project Overview, and Meeting Objectives

*Diana Foster, Society for Clinical Research Sites (SCRS)*

Experienced and productive site investigators are crucial to the success of clinical trials and the clinical research enterprise as a whole. However, there is growing evidence that the available pool of experienced site investigators in the United States is shrinking, with potentially negative consequences for clinical research. Without such investigators, the quality and efficiency of clinical trials may be affected. Further, high rates of attrition among site investigators place significant burdens on other investigators, research sponsors, and others who must shoulder the financial, logistical, and organizational burdens of initiating and training new investigators. But despite the seriousness of this issue, the reasons driving investigator attrition have not been fully explored, nor have potential solutions been proposed.

The Investigator Community Project (previously known as the "Investigator Turnover Project") was conceived by CTTI in order to better characterize and understand challenges faced by site clinical investigators and to issue recommendations that will help to strengthen and grow participation by productive, experienced site principal investigators (PIs) in the clinical research enterprise. Its two primary objectives are to:

1. Obtain a more thorough understanding of factors that influence investigators' decisions to leave or remain in clinical research practice; and
2. Facilitate an informed discussion of the challenges to, and strategies for, ensuring an adequate investigator workforce.

The project's anticipated impact is increased sustainability and decreased rates of attrition for the pool of experienced clinical investigators, leading in turn to improved efficiency in the start-up and conduct of clinical trials in the United States.

To further these goals, CTTI team members applied four primary project methods:

- Conduct structured interviews with investigators to determine barriers to remaining in clinical research, as well as possible solutions;
- Based on initial interview findings, conduct a survey of site investigators who left the clinical trial enterprise after a single trial ("one and done" investigators) in order to characterize issues contributing to investigator attrition;
- Interview currently active investigators to identify whether the challenges they have experienced in conducting site-based research are similar and/or different to "one and done" investigators, and to ask them to describe methods and strategies used to manage challenges; and
- Convene multi-stakeholder meeting of experts to discuss recommendations and strategies to address the concerns identified in the interviews and survey.

The results from these project methods are intended to inform the development of products including peer-reviewed manuscripts, workshop summaries, conference presentations, and a set of recommendations documents and associated implementation tools. These products will also be accompanied by extensive continual efforts to drive adoption of recommendations and tools by stakeholders such as sites, sponsors, CROs, academic research organizations (AROs), and others.

The specific objectives for the Expert Meeting in Silver Spring encompass the following:

- Present findings from CTTI's Investigator Community Project, including expert interviews and survey results;
- Receive feedback from meeting participants on identified challenges experienced by investigators and strategies to overcome these challenges;
- Identify essential elements necessary to strengthen and grow the community of productive, experienced site investigators;
- Develop strategies and best practices to promote the growth and strengthening of the community of experienced site investigators; and
- Identify barriers to strategy implementation and propose solutions.

## SESSION I: PRESENTATION OF PROJECT FINDINGS

*Facilitator: Diana Foster, Society for Clinical Research Sites (SCRS)*

### Session I Objectives:

- Present findings from "One and Done" survey
- Present findings from "Active Investigator" interviews
- Discuss findings, barriers, and solutions

### "One and Done" Survey Design and Findings

*Christopher Fordyce, University of British Columbia*

Christopher Fordyce presented findings from the "One and Done" survey, which was performed in order to learn why some physicians who initially decided to participate in clinical trials only did

so once, ceasing participation as a clinical investigator after only a single trial ("one and done" investigators). Specifically, the survey was designed to identify:

- Barriers to conducting FDA-regulated drug trials;
- Barriers that affected investigators' decisions to stop conducting such trials;
- Possible solutions that would enhance the experience of conducting such trials; and
- Benefits of conducting such trials.

The FDA's Bioresearch Monitoring Information System (BMIS)[*] was used to identify 34,001 US-based investigators who had submitted only one FDA Form 1572 within the past 15 years (1999-2014). Of these investigators, 20,000 were randomly sampled and their names and contact information provided to a consulting firm to locate their email addresses (investigators' email addresses are not included in the BMIS database). A total of 2,900 investigators with active email addresses were identified and sent the survey questions. Approximately 200 responded to the survey; of these, a little over half were identified as "one and done" investigators. Responding to questions about overall reasons for discontinuing research activities, the largest proportion of survey participants (45%) indicated that they wanted to continue performing clinical trials but lacked opportunities to do so. Respondents who indicated that they had made a personal decision not to continue or had discontinued for other reasons or specific barriers accounted for 29% and 27%, respectively.

### *Reasons for Discontinuing Research: Hypothesized vs. Actual*

CTTI investigators also incorporated into the survey six major hypothesized reasons for investigators wanting to discontinue research activities: 1) burdens arising from investigator and staff involvement and investment of time and resources; 2) time commitments, including time need to support trial conduct and prepare for study set-up; 3) financial issues, including contracting, budgeting, and payment schedules; 4) balancing trial commitments with demands of other activities; 5) difficulties in adhering to study protocol and procedures; and 6) burdens created by the amount, method, and frequency of data and safety reporting required. Each reason was presented in sequence during the survey. If the respondent

| Reasons One and Done Investigators No Longer Conduct FDA Regulated Drug Trials |
|---|
| Time to lead trial takes away from other necessary activities<br>• Long work hours<br>• Unpredictable work hours<br>• Trial demands make it difficult to devote time to clinical/non-clinical activities and activities supporting academic promotion |
| Too much time required to lead trial<br>• Amount of time to implement trial in general<br>• Time required by investigator to support trial and staff<br>• Amount of time required by staff to support trial<br>• Amount of time required to prepare for trial set up |
| Data & safety reporting<br>• Amount<br>• Method<br>• Frequency |
| Finance<br>• Sponsor/site contract negotiations<br>• Sponsor/site budget negotiations<br>• Final contract<br>• Final site budget<br>• Schedule of site payments |

[*] US Food and Drug Administration. Bioresearch Monitoring Information System (BMIS). Available at: https://www.fda.gov/drugs/informationondrugs/ucm135162.htm

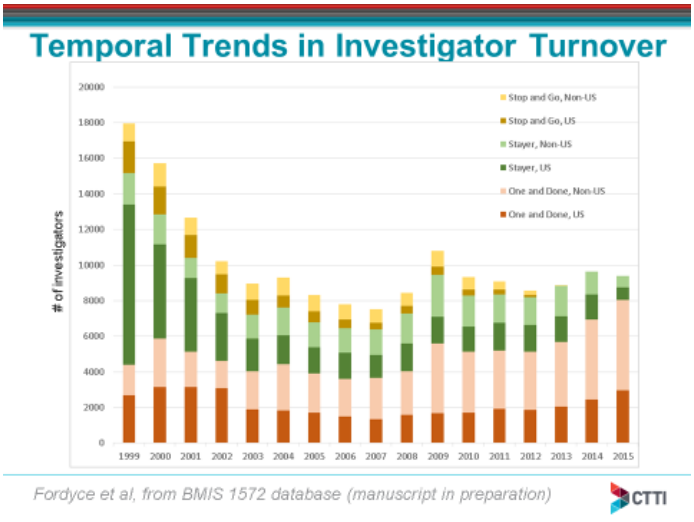
affirmed that any of these reasons presented a barrier in their experience, they were asked to provide additional detail; otherwise, they were presented with the next reason in the sequence.

Out of these six categories, survey responses indicated that issues presented by time commitments, balancing trial obligations with other activities, and data and safety reporting loomed largest for investigators (in that order), with financial issues taking fourth place. In addition, anecdotal statements offered by respondents reflected concerns about excessive effort, inadequate support, bureaucratic barriers, and lack of recognition and acknowledgment.

Taken together, these results suggest the need for further discussion about burdens related to trial setup and conduct, the multiple commitments balanced by site-based researchers, and whether additional financial compensation might potentially offset some of these burdens. A detailed summary of these findings has recently been published in the journal *Contemporary Clinical Trials Communications.*[†]

In addition, Dr. Fordyce presented data from an investigation that establishes distinct "phenotypes" for site investigators involved in FDA-regulated drug trials: "one and done" investigators; "stop and go" investigators who conducted multiple trials separated by substantial intervals; and "stayers" who remained continuously engaged in performing trials throughout the study period. This study, which also used data drawn from the FDA's BMIS database, applied percentile scores to identify active vs. inactive investigators based on the filing of FDA Form 1572 (a necessary precondition to performing FDA-regulated drug trials as a PI). It also examined temporal trends in investigator participation by geographic region (US- vs. non-US based). The study, which is currently being prepared as a manuscript for submission to a peer-reviewed journal, yielded the following key findings:

- Over the study period (1999-2015), the number of clinical trial investigators submitting FDA Form 1572 declined by approximately one-third;
- Investigators were more likely to have participated in only a single clinical trial ("one and done" investigator) compared with multiple trials ("stop and go" and "stayer" investigators);
- A temporal shift from predominately US-based investigators to non-US-based investigators was observed across all subgroups.




[†] Corneli A, Pierre C, Hinkley T, et al. One and done: Reasons principal investigators only conduct one FDA-regulated trial. *Contemp Clin Trial Comm*. 2017;6:31-8. http://dx.doi.org/10.1016/j.conctc.2017.02.009

## Active Investigator Interview Findings

*Terri Hinkley, Association of Clinical Research Professionals (ACRP)*

Following Dr. Fordyce's presentation, Terri Hinkley presented complementary findings from a study of physicians who have remained consistently active as site investigators for FDA-regulated drug trials. In this study, a total of 23 investigators identified as "active" (i.e., those who had served as a PI in a minimum of four distinct FDA-regulated drug trials in the two years prior to June 1, 2016) were interviewed about their experiences as a site PI. Interview questions included queries about whether the investigators had encountered challenges during their research efforts and if so, were asked to describe them in greater detail. Interview subjects were also asked for their impressions about factors associated with success as a site PI.

The 23 interview participants were roughly equally distributed among community-based researchers (n=8), site-based researchers (n=8), and academic investigators (n=7). Participants were identified using information from the BMIS database, which Ms. Hinkley reminded the group could provide only an incomplete snapshot of the larger clinical trials enterprise, as it encompasses only some investigators, and of those, only ones who are involved with FDA-regulated drug trials.

The two primary objectives of the study were to:

1. Identify reasons active investigators have been successful at participating in multiple FDA-regulated drug trials; and
2. Identify challenges experienced or avoided by active investigators in the conduct of FDA-regulated drug trials and describe the strategies used to manage and/or prevent these challenges.

Responses from study participants indicated that most received their first experiences in clinical research during fellowships or as a sub-investigator, in both cases under the leadership of the PI. A smaller proportion had immediately served as PI. Almost all respondents indicated that they learned about research opportunities from direct contact from sponsors, with many noting that reputation was a factor in being solicited to participate in trials. Other means for accessing research opportunities included participation in research networks, direct outreach to industry sponsors, and personal networking.

### *Key Factors in Investigator Success*

Respondents identified a number of elements as important to a successful career as a site PI. Access to **experienced, well-trained staff** was cited as a critical component of success, with the position of study coordinator being noted as particularly important. Other key staff included administrative personnel, regulatory experts, research nurses, data and IT support, budget and contracting experts, and research pharmacists. **Personal commitment** and a strong **work ethic**, as well as a capacity for enjoying the demands of the work, were also cited. **Institutional support** (including assistance with budgeting and contracts, protected time for research activities, and physical space) was another important element, as was the **ability to recruit patients** to the study (defined by two key dimensions: ability to accurately assess available patient populations and knowing when to decline infeasible studies). **Business knowledge and experience**, a **strong reputation** as a successful researcher, the **ability to network**

**effectively**, and a **realistic outlook** when selecting protocols/recruitment approaches were also considered important to success.

### *Challenges Confronting Investigators & Strategies for Avoiding/Overcoming Challenges*

When asked to describe the most significant challenges facing them in conducting clinical trials, investigators consistently identified four major issues:

1. **Trial finances**‡, including tight budgets (mentioned much more often than any other finance-related issue), trends toward less compensation for more work, and challenges related to budget negotiations, payment delays, inaccurate budgeting by study team, and competition from CROs for limited funds;
2. **Time required to implement the trial**‡, including factors such as: time needed to conduct trial greater than originally anticipated, need for additional staff/effort exceeding original plan/budget, extreme difficulties in negotiating for coverage, and delays in starting trial;
3. **Data and safety reporting**, including the volume of required reporting for adverse events/serious adverse events, time required to meet reporting needs, the number of adverse events requiring signoff by the investigator, and the volume of requested information from sponsors and/or CROs/monitors; and
4. **Workload balance**, including time taken away from other activities and issues related to salary coverage.

Other frequently cited challenges were difficulties related to **patient recruitment** and overly stringent or complex **eligibility criteria**; problems related to **CROs and sponsors**, including poor-quality staff, high rates of turnover among monitors, inflexible/poorly trained monitors, misaligned incentives, and communication issues; and research **protocols** that are unclear, of poor quality, and/or do not reflect an informed understanding of the realities of the clinical practice setting.

### *Recommendations for Becoming an Active Investigator*

Interview participants offered suggestions and recommendations for staying engaged as a successful site principal investigator and overcoming challenges:

- Engage in educational and training programs, including professional organization conferences, institutional offerings such as lecture series, and degree programs focused on clinical research;
- Network with experienced investigators and/or find a mentor;
- Serve as a sub-investigator on a clinical trial;
- Look for available trials;
- Establish realistic expectations;
- Plan adequately before committing to a trial, including by assessing trial feasibility, assuring a sufficient patient population, and fully understanding the PI's roles and responsibilities;
- Create a realistic recruitment plan; and

‡These challenges were also frequently cited by "one and done" investigators.

- Assemble qualified, experienced study staff (with the study coordinator being particularly important).

## Open Group Discussion

An open discussion by all meeting participants followed these presentations, during which the following major points were raised and discussed:

### *Difficulties Gaining Access to Trials*

One investigator from a small private practice described difficulties in recruiting patients and in gaining access to trial opportunities from sponsors/CROs despite creative efforts—something that was perhaps due to not meeting a preconceived notion of what a "perfect" investigator or site would look like. At the same time, sponsor representatives indicated that despite programs to bring new investigators into clinical research, approval of less experienced investigators was still proving to be a limitation, despite the provision of infrastructure.

One finding from the survey data that was noted as surprising to some participants was that so many "one and done" investigators wanted to do additional trials, but were unable to find studies open to them. Other data suggest that site selection in clinical research is weighted toward established/experienced sites. Metrics showing that only about 30% of sites are "new" investigators imply that the enterprise as a whole is not succeeding in bringing new sites into clinical trials. One participant reported difficulties recruiting patients despite enthusiasm for research among investigators at her institution as well as a vetting program to ensure the viability of trials. Another participant suggested that in many cases, patients are waiting to get into trials and providers are interested in participating in studies, but problems arise in finding ways to reliably and efficiently ensure that sites, trials, and patients all connect.

### *New Investigators: Risks and Challenges*

One participant noted that from industry's perspective, new investigators represent a risk to the study sponsor. The quality of the study at a site run by an inexperienced investigator may be poor; the investigator might not know how to deal with protocol deviations or follow through in a timely fashion. Another participant noted that the risk associated with inexperienced investigators is granted, but that questions about sustainability and strategic objectives remain—how else can the next "generations" of investigators be cultivated if they cannot gain experience working on trials? There was agreement that this was true and that industry definitely tries to develop new investigators, but risk is still an issue for sponsors, and about one-third of investigators don't do well.

A representative from the FDA noted that the agency sees both the good and bad through responses to Form 483s[§] and compliance letters. The overarching theme that emerges is the need for a reliable network of commitments among investigators, staff, patients, CROs/monitors, and sponsors. Effective conversations about capabilities and needs are key.

[§] See here for information about FDA Form 483: https://www.fda.gov/iceci/inspections/ucm256377.htm.

### *The Need for Supportive Infrastructure*

One participant noted that geographical differences, including attitudes toward collegiality, may play a role. In addition, the consolidating of smaller practices under larger institutions or health systems affects dynamics, and raises questions about how clinic-based research can proceed when hospitals and health systems are absorbing so many private practices. Is it possible to reach residents and early-career physicians before the pressures of practice compete too much for attention? Trying to run a smaller site successfully in a sustainable fashion is challenging especially because of finances. But we *can* sustain training programs to target residents and early career physicians, perhaps even at medical school. Such a training program could focus not just on the academic perspective but also include the private-practice side.

One meeting participant shared their larger system's experiences in integrating research into clinical care. They found that despite excellent academic investigators, large patient populations, and spending to support research, infrastructure was still needed. Experienced and disciplined support staff were brought in to build capacity. Investigators are compensated according to relative value units (RVUs).[**] Avoiding overlap among studies is important, and sometimes tough choices must be made. Regulatory compliance and good clinical practice (GCP) standards also must be integrated. Adding academic conferences allows work to be shared and provides a look at the science behind the trials, helping to increase interest and engagement in research.

### *Leveraging Technology and New Approaches*

Surveys and feedback suggest that it is important for both trialists and sponsors to be creative in their approaches to site-based research, and sponsors in particular are thinking critically about existing conceptions regarding where patients are to be found, and what constitutes a research site. Some sponsors are interested in using electronic health record (EHR) technology to turn the standard recruitment model on its head by first identifying sites where potentially eligible patients can be found, and then approaching providers to ask if they want to be investigators. It was noted the National Patient-Centered Clinical Research Network (PCORnet) is making inroads with these kinds of innovative approaches, which are helping to "democratize" clinical research. Also, from the perspective of the patient advocate, many of the issues presented seem to offer "low-hanging fruit" that could be swiftly addressed to improve the current state of clinical trials.

### *Delays in Study Start-up and Protocol Quality Issues*

The very large proportion of trials that experience delays in study startup also became a topic of discussion. Meeting participants agreed that many of these delays originate in problems with protocol development, highlighting the need for physicians and study coordinators to provide feedback on feasibility issues that can "make or break" a trial. It was also noted that while the internet has in some cases created new opportunities for engaging and recruiting patients, the profusion of false or misleading information creates problems as well. In addition, data entry burdens have been transferred to sites, and inflexible rules about who is authorized to review or

[**] Information on RVUs and use in physician compensation is available at: https://www.ama-assn.org/practice-management/medicare-physician-payment-schedules

access certain items—for instance, allowing only the study PI to review IND safety reports—may be introducing inefficiencies.

### *Monitoring and Source Data Verification*

There is also confusion about how to implement appropriate practices for data collection. Many monitors insist on 100% source data verification and the printing and faxing of enormous volumes of paper (which have only grown since the introduction of EHRs, due to frequent redundancy and "cut and paste" chart entries) represents a practice that is both burdensome and unhelpful in terms of protecting patients or advancing research. However, it was also noted that scaling back monitoring efforts while also attempting to expand the ranks of relatively inexperienced investigators could itself raise problematic issues.

## SESSION II: IDENTIFYING ESSENTIAL THEMES AND PROPOSING SOLUTIONS

*Facilitator: Matthew Roe, Duke Clinical Research Institute (DCRI)*

### Session II Objectives:

- Examine high-level themes established from collected data
- Identify essential elements to strengthen and grow participation of productive, experienced principal investigators
- Discuss generalizability and actionable solutions

### Key Elements for Site Investigator Success: Infrastructure, Training, Staff Support, and Formalized Mentorship

*Matthew Roe, Duke Clinical Research Institute (DCRI)*

Dr. Roe began his remarks by underscoring the point that clinical research is done by a team, not just the individual investigator. He then provided an overview of processes for initiating new clinical investigators: 1) **educational and training programs**, including conferences sponsored by professional organizations, institutional resources at academic centers, certificate programs in GCP, and specialized degree programs in clinical research); and 2) **apprenticeship opportunities**, including serving as a trial sub-investigator, participating on an institutional review board (IRB), becoming actively involved in financial and budget negotiations, and shadowing research coordinators as they conduct research activities.

Dr. Roe then presented a series of tables showing training elements available for research cardiologists as part of the Core Cardiology Training Symposium (COCATS) 4, which incorporates key competencies in clinical cardiology. He pointed out that the largest proportions of COCATS 4 training for cardiovascular research and scholarly activity were focused on research methods and procedural skills and knowledge, while there were no elements that specifically addressed site-based research.

### *Training for Site-Based Research*

In most cases, trainees are neither required nor encouraged to participate in site-based research, which is also typically de-emphasized at many institutions where participation as a site investigator in often not incentivized or rewarded with recognition. Given these challenges

facing new investigators, Dr. Roe asked participants to consider how such barriers can be addressed.

### *Institutional Infrastructure to Support Site Research Staff*

Where available, institutional resources, including centralized clinical research support, can be tapped by investigators. In such a scenario, institutional human resources management can hire talented, well-trained, and experienced trial staff. Other resources include regulatory expertise to review protocols and contracts and prepare for audits, coordinated GCP training, support for IRB submissions and contract negotiations, and templates for budgeting and accounting.

### *Practice-Level Support for Site Investigators*

Centralized research support resources like those available at larger sites or academic centers may not exist at smaller practice-level sites. National organizations may provide centralized support, but unless the research site is part of a large group practice within an integrated system, the ability to tap into these resources is likely to be limited. Likewise, financial, regulatory, and/or operational expertise may be difficult to find.

### *Time Requirements*

Time commitments and obligations for clinical research should be planned out in advance. Knowledge and experience are valuable when reviewing protocols to identify and plan for time commitments. In some cases, multiple ongoing trials may be necessary in order to keep full-time staff occupied. Time commitments for site-based research are rarely accounted for in investigator salaries, which are heavily weighted for individual research grants.

### *Actionable Solutions*

Actionable solutions to current gaps in training opportunities for site-based research include:

- Formalize training in site-based research at academic medical centers[††] and advocate for its inclusion in standard clinical training requirements for all specialties.
- Provide mentorship and apprenticeship opportunities for trainees and early-career physicians to facilitate “on-the-job” learning.
- Promote and create incentives for team-based research at institutions and within practices by leveraging institutional resources (when available) and leading by example (e.g., by recognizing team members and promoting a healthy and supportive environment for research).
- Work to solidify site-based research as a professional activity, not a hobby.

## Fiscal Responsibility and Discipline: Budgets, Negotiation, Payment Schedules, and Terms

*Kaitlin Malone, Amgen*

Kaitlin Malone provided a research sponsor’s perspective on the factors that go into building a clinical trial budget. Contrary to some impressions, as a sponsor budget negotiation, she does

[††] Academic centers are specified for this point because all they provide a touch point for all physicians (during medical school and postgraduate medical education).

not consider “lowballing” payment to sites an effective strategy; rather, they consider experienced and knowledgeable sites to be essential to success and want to develop a fair and responsive budgeting process. Although creating a study budget can be a complex undertaking, it is governed by several relatively simple criteria:

- Study budgets should compensate a site for work and services performed, such as protocol procedures and personal time of the PI/study coordinator.
- Study budgets may also contain funds for non-subject-related costs, such as IRB fees and administrative startup costs.
- A study budget must be within Fair Market Value (FMV).

The contract between the sponsor and the site is also characterized by several key attributes:

- It outlines the terms, conditions, and performance expectations for the execution and conduct of the trial;
- It is legally binding;
- It will differ in appearance and in number and kind of provisions, depending on the sponsor; and
- Sponsors typically want to finalize contracts quickly so that startup activities can commence.

The contract between the sponsor and the site serves as the trigger for other subsequent activities. Payment methods and schedules differ across sponsors, and sometimes even across different studies by the same sponsor. Payments are for work performed, and the schedule, methods, and amounts should be discussed upfront and all fees to be paid to the site should be explicitly detailed on the executed study agreement. Improving accuracy and speed of sponsor payments to sites remains a focus of ongoing efforts.

### *Challenges and Strategies for Mitigation*

Ms. Malone next presented a sponsor’s perspective on some of the key “pain points” that are likely to emerge during budgeting and contracting negotiations, along with strategies for mitigating these challenges (see Table below):

| Challenge | Solution |
|---|---|
| Tight budgets | Well-trained staff who:<br>• Review protocol/schedule of assessments and build their own cost assessment and supply justification<br>• Determine site personnel time<br>• Know site’s startup costs, fee schedule, overhead costs, and any non-subject fees<br>• Communicate with others at site regarding fees (e.g., PI, study coordinator, pharmacy, radiology)<br>• Leverage lessons learned from previous clinical trials<br>• Proactively question sponsor |
| Lengthy contract negotiations | Well-trained staff who:<br>• Support use of master agreements to shorten future contract negotiations<br>• Take time to understand contract terms and supply justification<br>• Identify and/or escalate any terms that are “deal breakers” & propose alternative language |

| Challenge | Solution |
|---|---|
| | • Communicate with stakeholders at site regarding contract terms (e.g. PI, study coordinator, financial department)<br>• Leverage "lessons learned" from previous clinical trials or contract negotiations<br>• Proactively direct any questions to the sponsor<br>• Are available and comfortable discussing contract concerns with sponsor |
| Delayed/outstanding payments | Well-trained staff who:<br>• Are identified to help follow up on payments<br>• Follow a budget for the duration of the study (e.g., are there annual costs to invoice for?)<br>• Understand the payment methodology, schedule, and timing upfront<br>• Understand budget line items<br>• Leverage "lessons learned" from previous clinical trials<br>• Proactively communicate concerns with sponsor |
| Site cash flow concerns | • Invoice for all non-subject-related fees to avoid leaving "money on the table"<br>• Identify a payment trigger that they control that will create faster payments<br>• Ensure that original budget realistically covers costs determined at the beginning<br>• Identify extra personnel work during the course of the study not adequately budgeted for at start<br>• Be aware of sponsor delay of payment that needs to be escalated |

Tight budgets were mentioned more often than any other finance issue raised by sites. Ms. Malone noted that although large changes to budgets are difficult to accommodate without adequate background information, if the site can justify those changes in detail, the sponsor can use that feedback to improve the process. She also addressed a point that had been raised earlier in the discussion to the effect that CROs assume a portion of the budget allocated by the sponsor for the study; in fact, this is handled by a separate budget.

Ms. Malone concluded by presenting a set of key takeaway points to help sites navigate the process of negotiating budgeting, contracting, and payment issues with sponsors:

- Contract negotiations and payment issues are a key source of concern and frustration for sites;
- Experienced investigators typically have the knowledge and skills to understand when to pass on a trial due to critical financial issues;
- Experienced and qualified support staff are essential to the success of contracting and budgeting processes;
- Sites are responsible for developing realistic study budgets and should be able to justify requests; and
- Early and frequent communication between site staff and sponsor is key to dealing with concerns and avoiding problems.

## Optimizing Trial Execution and Conduct: Recruitment, Protocol Eligibility, FDA Reporting, and Investigator Platforms

*Robin Douglas, QuintilesIMS*

Robin Douglas discussed data findings on challenges to executing and conducting site-based clinical research, along with some potential solutions. She began by noting that the complexity of clinical trial protocols creates a challenge for all stakeholders, and that one of the most effective strategies for dealing with this complexity is to ask questions upfront. Some key challenges from site perspectives included: 1) lack of quality and clarity of research protocols, 2) CROs creating a barrier between sites and sponsors, 3) high rates of turnover among both site and monitoring staff, and 4) poorly prepared clinical research associates (CRAs) who hinder study progress. She then presented some basic strategies to help ensure the success of study setup and conduct:

### *Prepare Prior to Trial Implementation*

Although finding the right people for the task can be challenging, sites should try to leverage knowledge and experience when reviewing protocols so that time commitments, basic feasibility issues, and potential challenges can be known in advance.

- If there are concerns about time commitments or logistical issues, this should be discussed with the sponsor in advance.
- Developing a realistic idea of time commitment, including anticipating likely delays, is important—although it is questionable whether these inefficiencies should simply be accepted or can be improved upon.
- Staff should not be assigned to a study until it is up and running.
- Review the protocol with an eye to feasibility, calling upon multiple reviewers with diverse perspectives to assess operational and patient population issues.
- Where possible, become involved in protocol development.
- Decline trials for which your site is not well-suited (contrary to widespread belief, such refusal does not prejudice the chances of the site or investigator being offered participation in other trials).
- Address potential barriers by recruiting patients from one's own practice, trying different recruitment strategies, and seek out the perspectives of patients/potential study participants.
- Communicate with sponsors and monitors, providing feedback and (where needed) requesting clarifications about trial design, protocol, and eligibility criteria.
- Discuss recruitment and screening challenges with sponsor, and develop and communicate reasonable estimates for accrual.
- Be proactive in looking for potential participants.

Regarding the impression that CRAs hinder study progress, Ms. Douglas noted that this issue reflects a chronic problem in clinical research—that there is typically more work than there are qualified personnel to do it. Anticipating turnover and encouraging retention can help ameliorate this. Further, although CROs were characterized by some sites as creating barriers to communication between sites and sponsors, it was pointed out that the core function of the CRO is to present a single point of contact; they are not meant to bar communications between sites and sponsors.

Each site is different, and as such will face different challenges. Sites should try to be creative in their approaches, plan for contingencies as much as possible, and partner and communicate with other stakeholders, especially patients. Finally, when the unexpected does occur, sites should communicate this to the CRO and sponsor, and press for support.

## Investigator Perspective: My Approach: Why Do I Remain Involved?

*David Whellan, Jefferson Clinical Research Institute*

David Whellan provided a personal perspective on why investigators seek out and remain engaged in conducting site-based research. He pointed out that such motivations are not necessarily static and often change over the course of an investigator's career. In addition, university or academic-center research differs in significant ways from research in a private-practice context, although there is also some overlap as well.

Dr. Whellan also noted that one cross-cutting inducement for engaging in clinical trials is that it allows investigators to offer cutting-edge treatments to patients, who often care about future benefits to other patients that derive from clinical research. In addition, patients typically receive high-quality care while participating in clinical trials.

Variety is another potential inducement for investigators, as clinical trials offer opportunities for experiences outside ordinary clinical care. However, the burdens associated with conducting trials tend to attenuate the satisfaction derived from those experiences. Career clinical research and its incentives in general are geared more toward academics than physicians in private practice. One problem, however, is that site-based research is typically not valued within academic practices, and finding sufficient bandwidth to conduct trials and keep dedicated staff sufficiently occupied can be a struggle.

The complexity of clinical research, including details of contract negotiations and budgets, presents a major challenge to participation. Building supportive infrastructure and placing an emphasis on training can help. Clinical research institutes may already provide access to resources that help faculty and staff conduct trials efficiently, but for other potential investigators, "roadshows" that demonstrate how to do clinical research are one possible solution. EHRs and patient portals offer ways to reach out directly to patients and providers. Consortia can be built to share and leverage resources across wider groups, as well.

## Open Group Discussion

### *Lack of Experience and Training*

One common theme across multiple presentations is the issue of research monitors who lack knowledge, training, and experience. (Re-) prioritizing high-quality training programs for monitors could help; it was noted that while recent trends have emphasized remote/virtual investigator meetings for investigative site personnel, in-person programs offer value as well and help generate enthusiasm for the study. The lack of formal training was also identified as a problem for study coordinators, one that can create a "perfect storm" when the monitor and investigator also lack experience. In the case of the latter, issues such as being "afraid to say no" to problematic studies, overloaded systems, a reluctance in some cases for more seasoned investigators to train or mentor junior investigators may all play a role.

### *Master Agreements & Study Protocols*

Master agreements, which can greatly expedite the process of contracting across multiple studies (by eliminating the need for continuous renegotiations of contracts), are sometimes neglected because the push to get individual studies up and running means that attention is not given to getting a master agreement approved. Problems with protocols are common as well. Clarity is often an issue; for instance, sometimes the protocol instructions don't match the study's schedule of assessments or require "surprise" assessments, leading to delays, amendments (with further delays), and budget problems.

**Possible recommendation:** creation of a templated set of key administrative elements for site-based research.

### *Fair Market Value*

The group also discussed the concept of fair market value (FMV) at length. FMV represents a benchmarked average estimate of the costs of procedures and personnel time that study sponsors use to create compensation ranges for site reimbursement. However, there were numerous questions about how FMV is derived and concerns about the lack of transparency around the creation of these measures, as the data used to create FMV estimates are typically proprietary and not easily available for scrutiny by sites.

Meeting participants representing sponsors and CROs indicated that for them, FMV estimates provide a preliminary window for developing a trial budget. However, individual circumstances at sites may offer rationales for adjusting payments. Sponsor representatives reiterated that budget estimates are not arbitrary: they do not wish to "lowball" sites and want the budget to be fair, but added that addressing variance and outliers is easier when sites have a well-developed rationale and data to justify a different rate of compensation.

Some investigators, particularly those from non-academic sites, noted that the lack of transparency around FMV estimates places them at a disadvantage. They pointed out that systems used by sponsors to generate study budgets (such as QuintilesIMS GrantPlan) are not available to individual investigators, nor is hiring a consultant a realistic option for smaller research sites/practices. They also noted that they have heard consistent anecdotal evidence that larger sites enjoy significant advantages in negotiating higher rates of compensation relative to smaller sites who lack the resources (or in some cases, "inside knowledge" about billing for administrative overhead) to compete in this arena, with the end result that smaller sites get paid less to do the same things.

### *Transparency Issues*

Continuing from the discussion about FMV, the group moved to a broader discussion about transparency, including why information such as the data used to calculate FMV was not more widely available, or even in the public domain? Some participants indicated that it seemed as if those most impacted by the decisions enabled by these data were least able to access it, while those from academic medical centers noted that the structure and culture of such environments created a different perspective on such issues than private practice might encounter. A patient representative observed that while sites and investigators were concerned about issues of livelihood, for patients the issues were more urgent, and in some cases might be a matter of life

or death. For patients, the end result of such negotiations is not just a piece of paper, but the ultimate effect on themselves and their families, and delays in getting a trial approved could have immediate human costs.

There was a general agreement that the issues raised were "global" ones that affect site-based research, albeit in different ways according to factors such as site size, available resources, and levels of experience. In addition, there was a general consensus that there was potential for identifying changes that industry can make to improve quality of the clinical research experience for all stakeholders. Although perfect agreement is unlikely, it should be possible to focus not on definitively fixing problems, but pivoting toward creating opportunities to fix problems.

## SESSION III: FDA PERSPECTIVE AND FEEDBACK

*Facilitator: David Ciavarella, CR Bard, Inc.*

### Session III Objectives:

- Provide FDA tools to help investigators succeed
- Examine FDA-identified concerns and areas for improvement

### A Primer in FDA Resources for Clinical Investigators

*Bridget Foltz; FDA, Office of Good Clinical Practice (OGCP)*

Bridget Foltz provided an overview of relevant FDA resources. She noted that although the agency does not promulgate nor enforce regulations in the area of investigator turnover and training specifically, it does maintain a website devoted to housing resources and information about GCP in general, some of which is directly pertinent to investigator training and site preparedness. The site includes links to regulations (including an electronic version of the Code of Federal Regulations Title 21 [21 CFR]) as well as preambles that contain useful background information, such as public comments from rulemaking process and FDA final analysis decisions. The site also hosts links and descriptive information for:

- FDA Guidances;
- Information sheets;
- International Conference on Harmonisation (ICH) guidance documents; and
- Proposed and draft FDA Guidances.

*FDA Webpage for Clinical Trials and Human Subject Protection:*

https:\\www.fda.gov\gcp

The most frequently referenced Guidances for clinical investigators on the website include those dealing with investigator responsibilities, frequently asked questions about the Statement of Investigator (Form FDA 1572), financial disclosure obligations, and the ICH E6 consolidated guidance on GCP.

The OGCP also offers a listserv that provides subscribers with automatic notifications about new guidances, regulations, and FDA webinars.

The FDA's GCP Program mailbox receives roughly 1200 inquiries per year, and FDA staff respond to general questions, although those with specific questions are encouraged to consult first with the study sponsor. However, if people have a question and don't know where to go, they are welcome to ask the OGCP.

The site also provides links to educational materials, including comparisons of FDA vs. Health and Human Services regulations, redacted emails (including original inquiries and replies) from the GCP mailbox, training information about GCP, and historical background information. FDA also sponsors a course in investigator GCP training; a links to the course as well as recordings and course materials are also available on the site.

Finally, the site includes links to information about the ClinicalTrials.gov registry and details about compliance obligations and enforcement policy.

### FDA Observations Related to Investigator Participation

*David Burrow; FDA, Office of Scientific Investigations (OSI)*

David Burrow presented his anecdotal observations of overarching characteristics that differentiate clinical investigators who stop after conducting a single study versus those who continue as researchers:

- **Role of the clinical investigator vs. the physician.** Working as a clinical investigator requires a change in mindset relative to serving as a physician only. Investigators have to sacrifice flexibility in order to adhere to a protocol and must work as a team member instead of having primary authority for judgment-based decisions.
- **Interests vs. needs.** The investigator must be able to understand and accommodate the sponsor's imperatives as well as their own, and understand their own responsibilities within this system.
- **Operational tension.** Investigators must learn to balance the need for speed and efficiency with quality and specificity in a context where subjects are receiving treatments that must be provided in specific, regimented ways.
- **Output vs. process.** Investigators must be able to understand the needs of the protocol and adapt their own practices to serve those ends—not attempt to circumvent the protocol or create ad-hoc workarounds.
- **Math.** PIs must understand how to "spend time to make time." In other words, if a project is to succeed, PIs must devote time to training personnel and sub-investigators on what success looks like and how to achieve it.
- **"Rules of Tetris."** Investigators must learn the rules of the game, and understand that perfection in clinical research is almost unattainable. Errors pile up, while accomplishments disappear.
- **Influence and trust.** In a typical scenario, the research site is owned by a third party; the investigator is employed by the site. The site may be "responsible" in the investigator's eyes, but the investigator is responsible under the regulations. Investigators should create and maintain a reliable network of commitments and read and understand any documents before signing them.
- **The protocol as the blueprint.** Protocols are the principal driver of the investigator experience, but there is wide variation across protocols. Investigators need to be sensitive to the nuances of language and aware of the need for clear and unambiguous language (for instance, "should/may/request" vs. "shall/must/required").
- **Systems.** Some institutions have robust systems in place for supporting research, while others do not. The former is set up for success, while the latter is set up for failure.

Sufficiently robust systems can help ensure compliance even investigators are not fully aware of their personal responsibilities.

- **Awareness and understanding**. Investigators should appreciate that at some point they will encounter problems. The key to success is resilience. Investigators should engage in clinical research with intent and be aware of processes, responsibilities, and rules. They should work to build systems and relationships that support success. The investigators who don't come to grips with this are typically the ones who fail and don't continue in clinical research.

## Open Group Discussion

Discussion focused on identifying opportunities for improvement in the system. While it was agreed that some things, such as the nature of informed consent and the strictures around it were unlikely to change, some of the overburden of data collection and monitoring that are shown to add little or no value could be pared away to create leaner, more efficient trials. However, it was also pointed out that risk-based monitoring approaches cannot simply be tacked on to a study, but must be built into the protocol and take into account the specific needs and exigencies of the study.

Discussion also revisited the problem of protocol development and the need to find ways to incorporate perspectives from knowledgeable experts and stakeholders so that impracticable or infeasible studies can be avoided. With the FDA pushing for the development of more pragmatic, streamlined trials, the question then becomes: how do we get there?

"Disruptive" undertakings such as PCORnet, which is seeking to improve the US capacity to conduct more efficient, streamlined, patient-centered trials provides one such vehicle. The overall objectives of PCORnet include the creation of generalizable tools, networks (including both academic data networks and patient-powered, therapeutic-area-focused networks), and policies that can build the foundation for a learning health system. One PCORnet program, the ADAPTABLE aspirin dosing trial[‡‡], is already piloting novel approaches that are changing conceptions about what constitutes a "site" or an "investigator."

[‡‡] See "ADAPTABLE, the aspirin study – A patient-centered trial." Available at: http://theaspirinstudy.org/.

## SUMMARY AND CLOSING STATEMENTS

In summarizing the day's discussions and presentation, it was noted that while there were relatively few surprises as such, there was a great deal of validation and clarification about the challenges faced in engaging and retaining clinical investigators. The importance of thoughtful follow-up and the development and execution of flexible recommendations that avoid being too prescriptive was emphasized.

A number of key themes emerged during discussions, and could serve as the basis for further work:

1. Clinical investigators and their study staff often have interest in and enthusiasm for conducting clinical research, but need access to training, mentoring, and supportive infrastructure (and in some cases, institutional support) to flourish as effective research sites.
2. Educational and infrastructural elements are not equally available across all clinical sites, with larger academic sites and large practices enjoying advantages relative to smaller practices, who sometimes struggle to establish themselves with research sponsors and CROs. In addition, specific training in site-based research is lacking among national training curricula.
3. Expanded access to education, training, mentorship, and supportive resources for investigators and staff are needed across the spectrum of research, but especially so for smaller practices and individual researchers who lack access to academic center resources.
4. Increased communication, education, and transparency around issues such as contracting, budgeting decisions, and site recruitment could benefit investigators and improve interactions with sponsors and CROs.
5. Incorporating input from all stakeholders, including patients and experienced study personnel, can improve the process of protocol development, improving the overall trial experience and reducing delays in study startup.

## FUNDING STATEMENT

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## ABOUT CTTI

The Clinical Trials Transformation Initiative (CTTI) is a public-private partnership to identify and drive adoption of practices that will increase the quality and efficiency of clinical trials. The CTTI vision is a high-quality clinical trial system that is patient-centered and efficient, enabling reliable and timely access to evidence-based prevention and treatment options.

## APPENDIX A. MEETING AGENDA

# Strengthening the Investigator Site Community Project

*Formerly Known as the Investigator Turnover Project*

## Agenda of the Multi-Stakeholder Expert Meeting

## April 5, 2017

Sheraton Silver Spring Hotel
8777 Georgia Avenue
Silver Spring, MD 20910

CTTI MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials

### MEETING OBJECTIVES:

- Present findings from CTTI's Strengthening the Investigator Site Community Project: Expert Interviews and Survey
- Receive feedback on identified challenges experienced by principal investigators and strategies to overcome these challenges
- Identify essential elements necessary to strengthen and grow the community of productive, experienced site investigators
- Develop strategies and best practices to promote the growth and strengthening of the community of experienced site investigators
- Identify barriers to strategy implementation and propose solutions

## WEDNESDAY APRIL 5, 2017

| | |
|---|---|
| **7:45 AM** | **Breakfast** *(Provided)* |
| **8:30 9:00** | **Introduction and Background** |
| 8:30 | Introduction to the Clinical Trials Transformation Initiative<br>*Gerrit Hamre, Clinical Trials Transformation Initiative (CTTI)* |
| 8:40 | Issue, Project Overview, and Meeting Objectives<br>*Diana Foster, Society for Clinical Research Sites (SCRS)* |
| **9:00 10:30** | **Session I: Presentation of Project Findings** |
| | *Session I Facilitator: Diana Foster, SCRS*<br>*Session I Objectives:*<br>► Present findings from One and Done survey<br>► Present findings from Active Investigator interviews<br>► Discuss findings, barriers, and solutions |
| 9:00 | One and Done Survey Design and Findings<br>*Christopher Fordyce, University of British Columbia* |
| 9:30 | Active Investigator Interview Findings<br>*Terri Hinkley, Association of Clinical Research Professionals (ACRP)* |
| 10:00 | Open Group Discussion |
| **10:30** | **Break** *(Refreshments Provided)* |
| **10:45 12:15** | **Session II: Identifying Essential Themes and Proposing Solutions** |
| | *Session II Facilitator: Matthew Roe, Duke Clinical Research Institute*<br>*Session II Objectives:*<br>► Examine high level themes established from collected data<br>► Identify essential elements to strengthen and grow participation of productive, experienced principal investigators<br>► Discuss generalizability and actionable solutions |
| 10:45 | Key Elements for Site Investigator Success: Infrastructure, Training, Staff Support, and Formalized Mentorship<br>*Matthew Roe, DCRI* |
| 11:00 | Fiscal Responsibility and Discipline: Budgets, Negotiation, Payment Schedules, and Terms<br>*Kaitlin Malone, Amgen* |
| 11:15 | Optimizing Trial Execution and Conduct: Recruitment, Protocol Eligibility, and FDA Reporting<br>*Robin Douglas, QuintilesIMS* |
| 11:30 | Investigator Perspective: My Approach / Why Do I Remain Involved?<br>*David Whellan, Jefferson Clinical Research Institute* |
| 11:45 | Open Group Discussion |

## WEDNESDAY APRIL 5, 2017 *(Continued)*

**12:15** **Lunch** *(Provided)*

**1:00 2:00** **Session III: FDA Perspective and Feedback**

*Session III Facilitator: David Ciavarella, CR Bard, Inc.*
*Session III Objectives:*

- Provide FDA tools to help investigators succeed
- Examine FDA identified concerns and areas for improvement

1:00 A Primer in FDA Resources for Clinical Investigators
*Bridget Foltz; FDA, Office of Good Clinical Practice*

1:15 FDA Observations Related to Investigator Participation
*David Burrow; FDA, Office of Scientific Investigations*

1:45 Open Group Discussion

**2:00** **Break** *(Refreshments Provided)*

**2:15 2:45** **Session IV: Panel Discussion Feedback from Participating Investigators**

*Session IV Facilitator: Matthew Roe, DCRI*
*Session IV Objectives:*

- Receive feedback from investigators on presented data and proposed suggestions to strengthen and grow the investigator community

**2:45 3:20** **Session V: Panel Discussion Identifying Potential Implementation Barriers to Overcome and Necessary Change Agents**

*Session V Objectives:*

- Identify strategies necessary to drive adoption of project recommendations
- Examine potential barriers to implementation and chart course to proactively address those barriers

Panel Participants:
*Terri Hinkley, ACRP*
*Diana Foster, SCRS*
*Matthew Roe, DCRI*

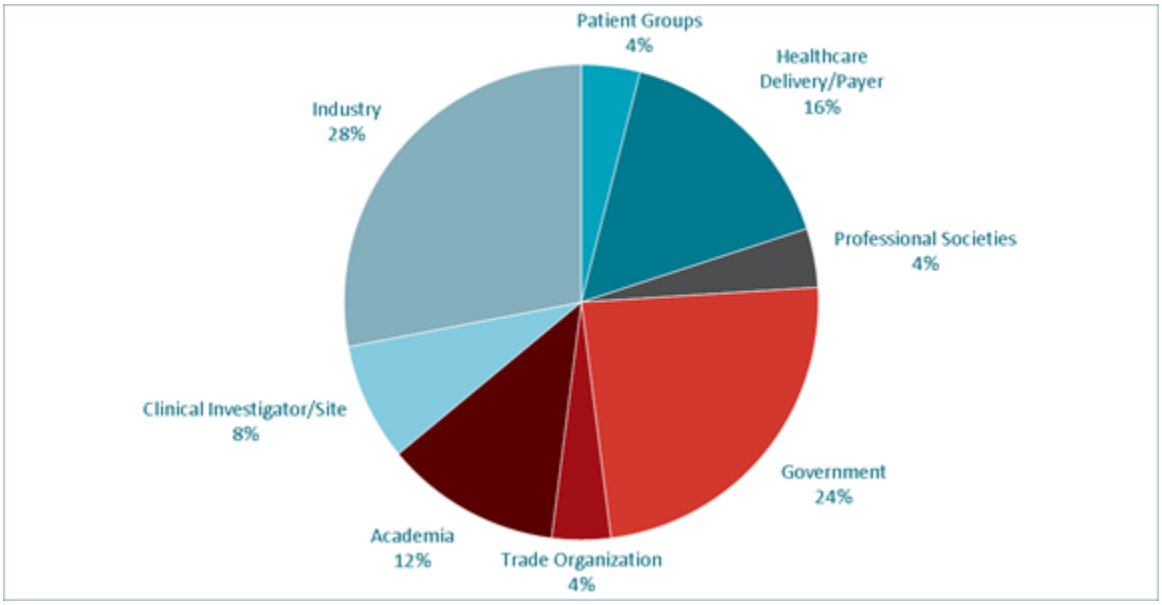
**3:20 3:30** **Session VI: Call to Action and Wrap up**

3:20 Closing Statements

**3:30** **Adjourn**

## APPENDIX B. MEETING PARTICIPANTS

Our meeting participants include representatives from a broad cross-section of the clinical trial enterprise including regulators, government sponsors of clinical research, academia, industry, patient advocates, clinical investigators, and other interested parties. Participants are expected to be actively engaged in dialogue both days.



## EXPERT MEETING PARTICIPANTS LIST

| Name | Affiliation |
|---|---|
| David Burrow | Food and Drug Administration, Office of Scientific Investigations |
| David Ciavarella | C.R. Bard, Inc. |
| Chris DeFilippi | Inova |
| Robin Douglas | QuintilesIMS |
| Molly Flannery | Food and Drug Administration, Office of Medical Policy |
| Bridget Foltz | Food and Drug Administration, Office of Good Clinical Practice |
| Christopher Fordyce | University of British Columbia |
| Diana Foster | Society for Clinical Research Sites (SCRS) |
| Melissa Heidelberg | Roche/Genentech |
| Terri Hinkley | Association of Clinical Research Professionals (ACRP) |
| Lindsay Kehoe | Children's National Health System |
| Joanne Krasnoff | Tenet Healthcare, Center for Advanced Research Excellence |
| Angela Kuramoto | Phoenix VA Health Care System |
| Elizabeth Mahon | Janssen |
| Kaitlin Malone | Amgen |
| Brock McConnehey | Northwest Clinical Trials |
| Providencia Morales | Phoenix VA Health Care System |
| Julio Paez | South Lake Pain Institute |
| Racquel Racadio | Amgen |
| Matthew Roe | Duke Clinical Research Institute |
| T.J. Sharpe | Patient Advocate, www.Philly.com/Patient1/ |
| Janice Sullivan | University of Louisville |
| Susan Taylor | Janssen |
| James Welker | Anne Arundel Health System Research Institute |
| David Whellan | Jefferson Clinical Research Institute |
| Todd Wilson | National Institutes of Health, NCATS |