The CenterWatch Monthly

February 2017 A CenterWatch Feature Article Reprint Volume 24, Issue 02

Reassessing site engagement activities

New approaches include earlier involvement, reducing burden, more permanent collaboration

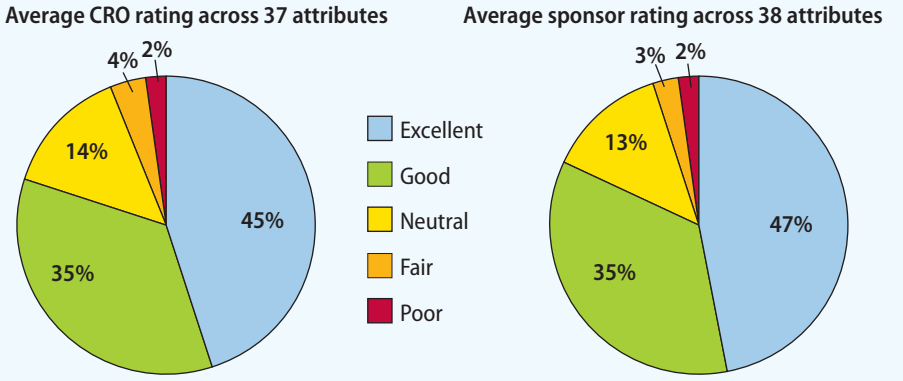
By Karyn Korieth

Drug development sponsors and CROs increasingly recognize the importance of investigative sites having a stronger, more respected voice in the clinical research community and have begun adopting initiatives designed to incorporate site viewpoints into improving clinical development processes.

Leading players, under increasing pressure to streamline R&D operations, have created programs that actively include investigators and site personnel early in the development process to solicit feedback on study design and execution. An increasing number of site networks and partnerships have also been formed that facilitate clear communication about issues that contribute to site burdens and allow for greater collaboration in developing solutions.

"Stakeholders are recognizing that sites are central to the drug development process and bringing new medicines to market. Close collaboration is essential in order to improve drug development timelines, cost and processes," said Tracey Gashi, executive director, Site & Patient Access, INC Research.

Average CRO and sponsor rating for relationship attributes



Source: CenterWatch, 2015; n=1,900 Investigative Sites

Additionally, the long-standing view of investigative sites as silent partners has begun to shift during the past five years as sponsors and CROs bring investigative site personnel together in forums or panel sessions, both in the U.S. and Europe, to discuss their perceptions about challenges and industry changes. Many companies work with the Society for Clinical Research Sites (SCRS), a global trade organization that represents more than 4,000 sites in 54 countries, to meet face-to-face with site representatives and understand their perspectives. Organizations also conduct surveys to gauge site satisfaction with clinical research teams and site engagement activities.

"There has been a huge improvement in sponsor and CRO relationships with sites during the past five years. They heard this was a need and have reached out to sites that are serious about doing research," said Mohammad A. Millwala, CEO of DM Clinical Research, a network of investigative sites based out of Houston, Texas.

Improving site engagement as part of patient centricity

Sponsors and CROs recognize that building stronger site relationships can lead to more predictable, higher-quality site performance. Yet initiatives to engage investigative sites have also been embraced as part of the patient-centricity movement. The greatest connection sponsors and CROs have with patients during the development phase is through investigative sites; awareness has grown about the fact that patient experience in clinical trials will not improve if organizations neglect their relationships with sites.

"Patients should play a more active role in clinical trial design and execution. Our goal is to optimize the patient experience. But you can't just think about the patient. You have to incorporate the various aspects of how the patient touches the study, which is through the site," said Abbe Steel, founder and chief executive officer of HealthiVibe, a company begun in 2014 to enable patient contributions to clinical trial design and patient initiatives. "The site is an important stakeholder."

Kim Ray, vice president, Site & Patient Networks at QuintilesIMS, added, "Many people are talking about the empowered patient and trying to understand how to work with the empowered patient in clinical research. Who better to help us understand that than the sites that work with patients every day? We can learn a lot from them."

Creating opportunities for early involvement

Efforts to understand study startup and execution from the site perspective have risen in recent years as increasing clinical trial demands have strained investigator relationships and increased site burden. Many of these difficulties are the result of the growing complexity of study protocols, which result in disruptive protocol amendments, longer cycle times and patient recruitment difficulties.

Given these challenges, sites have voiced a desire to share their experiences and be more actively involved in protocol design and study-execution discussions. Many sponsors and CROs, which have made improving their relationship with sites a top priority, have established or expanded site engagement departments and initiated programs that involve sites earlier in clinical development programs.

"Five years ago, nobody would ask sites to examine their protocol. Today, for some companies, the protocol analysis and examination with sites has become a standard operating procedure," said Mark Lacy, president and CEO of Benchmark Research, which operates six sites. "It saves huge amounts of time. Sponsors can design easier, more effective, more doable and less expensive studies by including the sites in protocol analysis. If sponsors ask sites about protocols before they are finalized, sites can say up front if they can't do something and sponsors wouldn't need so many protocol amendments."

Sanofi began an initiative in 2012, as a standard practice across all its R&D studies, to engage principal investigators (PIs) and clinical research coordinators during the study design phase. The process allows Sanofi to collect key information about aspects of the study that could make it more challenging to recruit participants, while it is still under development, so that those issues can be addressed proactively. Site representatives also provide detailed feedback on other aspects of the study, including considerations about how the study relates to and could improve the standard of care, information about the inclusion or exclusion of specific types of trial participants, comments on clinical trial procedures and options for patient-reported data collection. In addition, the investigators share non-proprietary information, as appropriate, about best practices that they've seen in other studies.

In January, Sanofi expanded its site engagement efforts to evaluate all aspects of its clinical trial execution to ensure its studies are a positive experience for both the trial site and the patient.

Since it initiated steps in 2012 to include sites more proactively in early study planning, Sanofi has seen a reduction, year over year, in its clinical trial recruitment timelines, and reduced its overall protocol amendment rate for clinical trials by more than half.

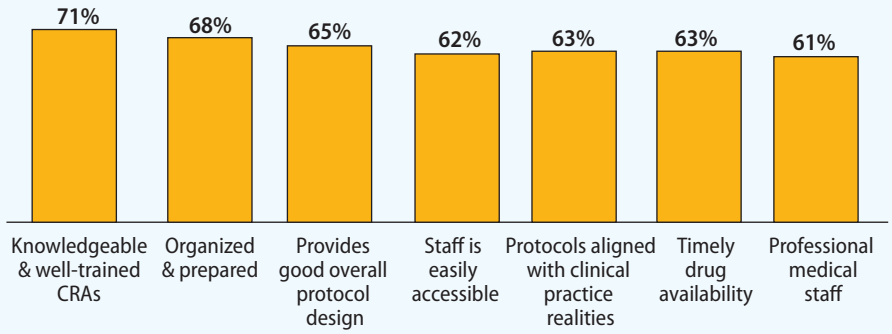
"A reduction in amendments is key because it is an administrative burden to investigators and their teams," said Victoria DiBiaso, global head, Clinical Operations Strategy & Collaboration at Sanofi. "Investigators and study coordinators are our partners in clinical research and it's critical to receive their input early in the design stages of the study."

Other sponsor companies, including Eli Lilly, have study teams watch simulations of clinical trial protocols before finalization to help identify potential issues investigators may encounter with the study design, complexity or feasibility. Patient engagement company HealthiVibe conducts simulations of screening or site visits, which employ site personnel and patients in mock clinical trial settings, to help sponsors understand how a protocol will be operationalized in a real-world setting. As part of the assessment process, site staff and patients are interviewed for feedback about the experience.

"The simulations allow the sponsor to stand up at the investigator meeting and say, 'We thought about what it's going to be like for you to sit down with a patient.' The sites appreciate that," said HealthiVibe's Steel, who has worked in the industry for more than 20 years. "Back in the day, sponsors just threw a protocol at the site and said, 'Get me patients.' Now sponsors think a lot about the burden on the site staff such as how long things take, how hard it is to log on to systems or how they need to deal with reimbursement for travel expenses. They have done a lot of work around what sites identify as the biggest burdens."

Most important relationship attributes

Percent rate 'Very Important'



Source: CenterWatch, 2015; n=1,900 Investigative Sites

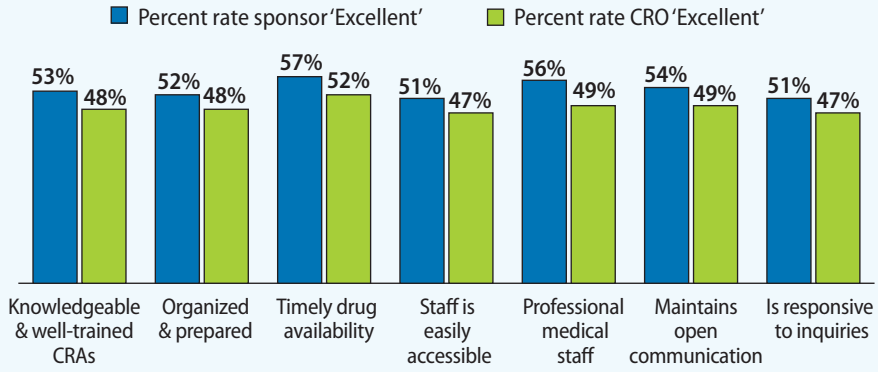
Preferred site networks allow for collaboration

A number of global CROs, which consider their ability to leverage site relationships an important competitive advantage, have established site networks or formed partnerships with top-performing sites that provide a means for establishing more sophisticated relationships and promoting greater communication between clinical teams and sites. The models typically designate relationship managers who are in regular contact with site personnel to review performance metrics, solicit site feedback and discuss upcoming pipelines.

QuintilesIMS, which 10 years ago established a pioneering Prime and Partner Sites program that includes 24 large institutions and more than 1,200 partner sites, has brought investigators together through its Site Vision Forum to discuss their perceptions about industry changes and ways to improve clinical research processes. Site feedback has been used in developing new programs or improving practices. Among the new programs at QuintilesIMS designed to reduce the burden of clinical trial participation is Qcare, which is a site services provider that manages research operations for a site, which are customized based on individual site needs, and can provide study coordinators or other research staff members. The CRO also negotiated with its sponsor clients for the ability to pay sites monthly on all new projects as a result of feedback from investigators about inefficient and lengthy payment processes.

"One of our strategic imperatives at QuintilesIMS is to improve the investigator experience. We've gained a lot of insight from our Prime and Partner Sites program that has helped us to enhance the experience of all sites," said QuintilesIMS' Ray. "It's important for us to have strong relationships with sites and understand their challenges so that we can do a better job on our end to deliver clinical research."

Comparing sponsors and CROs on common relationship attributes rated most important by investigative sites



Source: CenterWatch, 2015; n=1,900 Investigative Sites

QuintilesIMS also collaborates with its partner sites to evaluate new clinical research models. One project assessed the potential of using telemedicine in a hub-and-spoke model, which designated a central physician investigator and had primary care physicians from surrounding practices use telemedicine to conduct patient assessments.

"We have a lot of respect for our sites. We want to understand what they are facing and, from their perspective, where clinical research is going," said Ray.

Similarly, Novo Nordisk, which has consistently received high scores from investigators in the past three CenterWatch relationship quality surveys, invited study coordinators to a panel discussion about the site role in risk-based monitoring (RBM) and incorporated their insights into its new RMB program. For instance, the RMB model ensures that a team member evaluates why data analytics or algorithms flag a site for additional monitoring or auditing and then communicates directly with site staff rather than sending an automatically generated query. The study team member might discover that a high number of serious adverse events flagged through data surveillance techniques were the result of a patient being hit by a car, for example, rather than study-related incidents.

"It's more of a personal approach. It's leveraging systems technology and analytics, but still having that one-on-one relationship with sites to pick up the phone and have a chat once we've done our homework," said Kate Owen, vice president of Clinical Trial Management at Novo Nordisk. "We feel partnership with our sites is incredibly valuable."

In response to other site suggestions, Novo Nordisk partnered with a vendor to organize travel arrangements for clinical trials participants, rather than have sites manage the expenses and distribute travel stipends to patients themselves, and are working to simplify the paperwork needed for sites to verify that clinical trial supplies are stored at proper temperatures.

Parexel has made significant investments during the past three and a half years to engage investigators through its Site Alliance Network, which is comprised of more than 300 alliance member organizations and another 200 site management organizations. Quarterly face-to-face meetings are held with institutions and relationship managers are in contact with sites on a weekly or monthly basis.

"It's an incredibly competitive marketplace and we need to listen to investigators and to site staff simply because they are the direct access to patients. Without those investigators and understanding their needs, we aren't able to access patients for our clinical studies," said Dominic Clavell, vice president of Worldwide Site Strategy for

Parexel. "Over the last decade, many companies, including Parexel, have realized that they've got to invest heavily in long-term strategic relationships."

As investigators report that a key part of successful relationships with sponsors and CROs is the ability to count on a regular stream of work and more insight into upcoming pipelines, which would allow for more efficient resource planning, Parexel recently introduced a process called Straight to Startup, which streamlines how the CRO engages alliance member sites with new opportunities. Network sites can review Parexel's entire portfolio and choose the studies they want to pursue. If the site registers an interest and a capability for a particular study, Parexel immediately begins the qualification process.

"The qualification process is faster for the alliance network members than for other sites simply because we already know them so well," said Clavell.

In another example, INC Research began its Catalyst Program to not only better understand site needs, but also to establish a framework for collaborating with sites in order to streamline development processes and create new methodologies than can improve clinical research and site sustainability. Through the program, INC Research has worked with its Catalyst Site Network, which is a select group of high-performing sites from across the globe, to identify areas for potential improvement and developed revised processes and timelines that have led to significant efficiencies, particularly related to study startup. In response to site feedback, for example, non-core procedures have been taken out of protocols, wherever possible, and a more efficient approach to risk-based monitoring has been employed.

"By working in close partnership with sites in the Catalyst Program, we are able to understand the issues and burdens faced by sites and have developed solutions together," said INC Research's Gashi. "Understanding the site's perspective is critical to the success of our relationship."

Preferred approaches to receive information about clinical trials

	Non-participating HCP	Referring HCP	Clinical investigator
In-person at a meeting already scheduled	40%	75%	37%
At a separately scheduled meeting	24%	75%	21%
Via webinar	16%	N/A	5%
Via email	55%	50%	68%
Via printed material	38%	25%	37%

Source: PMG Research 2016; n=78 Healthcare providers

SCRS, formed in 2012, has also provided an important platform for sites to communicate their perspectives and issues. SCRS facilitates dialogue between site professionals and industry leaders through its Site Advocacy Group (SAG) initiative. SAGs, which typically are convened at the request of sponsors or CROs, have gained site input on a variety of topics including technology, operational processes, protocol feasibility and patient enrollment.

"Through the constant dialogue we are having with sponsors and CROs, we have witnessed real change among these stakeholders valuing the relationship with the sites. It is clear sites have options regarding who they choose to work with and are now being treated as partners, which is a welcome change and represents an absolute shift in culture—one we believe is permanent," said SCRS President Christine Pierre. "Sites are front and center in the mind of the industry, as they should be."

INC Research's Gashi added, "The CRO industry is now listening and acting upon this feedback."

Periodic assessments of engagement conducted

Sponsors and CROs conduct periodic assessments throughout clinical development programs to understand what sites identify as strengths or weaknesses in their site relationships and to gauge the success of various engagement activities. Organizations conduct their own internal evaluations, both through online surveys and face-to-face interviews, and contract with outside parties to provide independent assessments.

HealthiVibe, for example, polls investigators about which issues they feel are most important to address as part of sponsor site-engagement initiatives and has begun to develop an in-depth site survey, which will be launched later in the year, to collect site feedback.

"Sponsors want to invest the time and money for these activities because they want their sites to be partners with them. If it's a long study, they want to keep the sites motivated, engaged, educated and enthusiastic about the study. That is really critical," said HealthiVibe's Steel.

CenterWatch has introduced a new market research service, called the Collaborative Assessment Tool (CAT) Program, which collects and analyzes site assessments of how well clinical teams meet key relationship attributes on both a study-by-study and cross-study basis. Sites are introduced to the CAT Program at study startup and then contacted about completing the online survey at the end of the study. Sponsors distribute the survey results to sites and discuss the findings with site personnel.

"This type of measurement builds goodwill and further strengthens the sponsor/

CRO relationships with investigative sites," said CenterWatch COO Joan Chambers. "As the industry continues to move in the direction of patient engagement and patient centricity, the industry is also recognizing the equal importance of building and strengthening their relationships with investigative sites—a key player in reaching patients for participation in clinical trials."

Looking ahead

As the investigative site voice gains greater importance in clinical research, particularly as patient-centric drug development models continues to evolve, sponsors and CROs will need to reassess site engagement activities going forward and find new ways to not only listen to sites but also to incorporate their feedback into clinical development programs and practices. As competition for high-performing sites intensifies, investigators will choose to work with the organizations committed to soliciting their viewpoints and addressing site problems and concerns.

Changes underway in the site landscape will also require increased collaboration with investigative sites to understand new challenges that will arise. INC Research's Gashi said that as clinical trials increasingly move into community settings, for example, which may have limited experience in conducting research, investigators may require a greater amount of support to run clinical trials. In addition, a hub-and-spoke model may emerge where a regional PI oversees the trial, but study visits are conducted by a patient's treating physician, who may not be designated as a study investigator.

"The definition of a site is also likely to change in the future, not only with the ownership model of sites by CROs, but also with clinical research becoming a key care option within the healthcare system," said Gashi.

Going forward, sponsors and CROs will need to forge stronger relationships not only with investigators, but also with referring physicians who might not be involved in clinical research, particularly as the move toward personalized medicines requires smaller patient sub-populations. The need for industry to understand the needs of referring physicians was underscored in a survey conducted recently by PMG Research that found 75% of referring physicians surveyed, along with 67% of physicians who don't participate in clinical trials, indicated a desire to receive more information about the benefits of clinical research.

"The industry, as a whole, needs to take responsibility for prioritizing clinical trial awareness not just to patients, but also to the healthcare community," said Jennifer Byrne, CEO of PMG Research. "Physician engagement is the last piece that we need to better connect all the dots: It's not just a physician engagement strategy, a patient engagement strategy and a site engagement strategy. These groups have to work in harmony together."

Karyn Korieth has been covering the clinical trials industry for CenterWatch since 2003. Her 30-year journalism career includes work in local news, the healthcare industry and national magazines. Karyn holds a Master of Science degree from the Columbia University Graduate School of Journalism. Email karyn.korieth@centerwatch.com.