



What bothers clinical investigators?

A new survey of more than 1,000 clinical trials investigators working in the US reveals some predictable and some surprising concerns regarding their ability to function in an increasingly costly and complex trials environment, reports **Harold E Glass**.

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As the industry struggles with declining productivity as evidenced by the decreased number of submitted New Drug Applications (NDAs) and approved New Molecular Entities (NMEs), pharmaceutical management is examining every aspect of the R&D process to bring commercially attractive new drugs to market in a more timely fashion. The longest and most costly step in the entire process is late phase clinical research. The performance of investigators at clinical trial sites is a major issue for many involved in late phase development. TTC LLC and the University of the Sciences in Philadelphia (USP) are conducting an extensive, multi-year, global analysis of why some clinical trials finish faster and perform better than others do, including the operations of clinical sites.

Drug development organisations that understand and learn from the concerns of clinical investigators will be in a better position to design, and subsequently execute, quality

clinical trials in a more rapid time frame. A mail and email survey of over 1,000 US investigators reveals that investigators' operational concerns centre on financial management, drug safety reporting, and patient recruitment. These concerns are found in almost all types of active clinical sites and are not concentrated in one particular group or groups of clinical investigators. While investigator uneasiness with financial issues and patient recruitment may be what many would expect to see, their uneasiness with adverse event reporting is a potentially major issue.

Finance Matters

Investigators, as we might expect, are concerned about financial issues, ranging from developing accurate forecasts to cash flow. In fact this is their greatest general area of discomfort. We know that next to the desire to participate in medically innovative research, financial remuneration is the most important reason these

physicians take part in clinical research.¹ Yet many clinical sites are not comfortable with their ability to develop study budgets or track actual costs against those budgets. Nearly one-third of the sites have difficulty tracking costs against a budget. A slightly smaller number of sites point to their difficulties in developing an accurate study budget against which to track actual costs. A quarter of sites are bothered about the timely collection of invoices against milestones. Particularly noteworthy is that these concerns are found at all types of centres, including teaching and non-teaching hospitals, academic medical centres, and office-based practices. Large, sophisticated sites, and smaller, less experienced sites are all tested by the financial management of clinical trials.

Table 1: Percent indicating dissatisfaction with a financially related clinical trial activity

Tracking clinical trial costs against the budget	30
Accurately forecasting study budget	27
Timely collection of billables against milestones	26

According to one Midwestern investigator: "Internal billing and collection processes are difficult and payment from sponsors is not always timely".

Similarly, a Pacific Coast physician wrote that: "Based on current industry practices, it is almost impossible to track milestone payments to ensure that all study visits/procedures are being reimbursed".

Drug Safety Reporting Is A Worry

The uneasiness among investigators about the reporting systems associated with serious adverse events (SAE) is especially noteworthy. More than one-quarter of the clinical investigators are troubled by the SAE reporting systems in clinical trials, although far fewer have an issue with the follow-up activities of reported SAEs. The issue of drug safety has most certainly been the focus of great attention in the last few years, possibly highlighted by the Vioxx controversy. Investigators may be more sensitive to the general drug safety issue because medical professionals, public officials, and the general public have given the topic such attention. For example, the FDA has recently reorganised to provide more safety surveillance of marketed drugs, and a widely read Institute of Medicine report highlights the difficulty of anticipating possible drug safety issues with marketed drugs based upon the relatively small number of patients taking part in clinical research studies.² Whatever impact this increased attention on drug safety may have had among drug development professionals, US

clinical investigators are concerned about SAE reporting.

An experienced clinical investigator commented: "I worry about how we report adverse events. The issue has become more and more important for everyone. If I can't be sure if these reports get to the right people quickly enough, I am going to be careful which trials I accept."

Patient Recruitment is A Problem

Many drug development professionals consider patient recruitment to be a major obstacle in completing successful clinical trials in a timely manner. For a substantial minority of sites patient recruitment is an important operational issue.

A Washington DC investigator succinctly stated the concern: "Difficulty in recruiting participants is the major snag in performing these studies".

A Texas physician echoed the sentiment: "We have been participating in clinical trials since 1991 and if there was anything that is difficult for us, it is patient recruitment. I would like to have a better system in place for recruitment."

Investigators are less dissatisfied with other areas such as the amount of time the study monitor spends at the site. Even smaller numbers are dissatisfied with what they are expected to do for tracking clinical trial supplies or conducting study close-out activities.

A CRO Effect?

The use of contract research organisations (CROs) to conduct clinical trials has become a widely accepted aspect of drug development. Moreover, CRO usage will probably continue to increase.³ Some investigators may prefer to work directly with sponsor companies rather than CROs, although most investigators are actually fairly indifferent.⁴ However, the amount of work a site does with CROs is not related to a site's levels of dissatisfaction with the major operational aspects of clinical research. Sites that do a great deal of work in sponsor company-managed studies are no more or less dissatisfied with the operational aspects of clinical research than are those who do a substantial percentage of their work with CROs.

Table 2: Percent indicating dissatisfaction with other aspects of clinical trial activities

SAE reporting	26
Patient Recruitment	22
Study monitor time at sites	12
Tracking clinical trial supplies	9
Study closeout	8
SAE follow-up	5
Patient Retention	4

Now What?

We are currently examining investigator concerns in other geographies including Europe, Asia and Latin America. However, we know that US sites of all types continue to grapple with financial issues. And some sites are looking for better ways to recruit patients. A surprisingly high, and potentially troubling, number of investigators of all types are not comfortable with the SAE reporting processes. Pharmaceutical companies need to understand the sources of this SAE reporting discomfort. Clinical investigators unhappy with SAE reporting may be less eager to enroll patients for all, or some, types of clinical trials.

Sponsor companies and CROs who understand – and learn from – the operational concerns of clinical investigators will be better able to recruit and retain investigators. An investigator's experience with an organisation will affect their likelihood of taking part again in a study managed by the organisation. Just as importantly, learning from the collective experience of clinical investigators will help sponsor companies and CROs design better studies and complete them more quickly. Conducting clinical trials is an increasingly complex and costly task. Overlooking what investigators have to say on the operational challenges they face will not prove helpful.



References

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