Denise Myshko

Where Have *All the* Investigators Gone?

Sponsors' unrealistic practices are causing clinical investigators in North America to flee the field.

The investigative site landscape has become highly fragmented and unstable with high turnover rates, declining numbers of experienced professionals, and limited infrastructure.

More than half of all clinical trials worldwide that are regulated by the FDA were conducted by independent, community-based principal investigators, as opposed to universities, hospitals, and government clinics, according to a March 2013 study released by the Tufts Center for the Study of Drug Development.

While the proportion of community-based investigators worldwide has grown, site performance has been exceedingly variable due, in part, to the limited experience and scale established by sites outside North America, according to Tufts CSDD. The landscape is also less stable, as turnover rates remain high, particularly in regions outside North America.

In North America, the number of investigators is declining. Almost 28,000 investigators around the world participated in clinical studies in 2012, with 61% of them based in North America, down from 84% in 1996.

The number of veteran investigators is also declining at a rate faster than other segments, according to a CenterWatch report last year. This study looked at those who filed 1572 forms, which the FDA requires from investigators at the beginning of each study. The number of investigators who filed two such forms each year dropped from 29% to less than 23% over the previous five years. Additionally, more than 40% of all investigators who signed a 1572 form in 2006 never returned to clinical research.

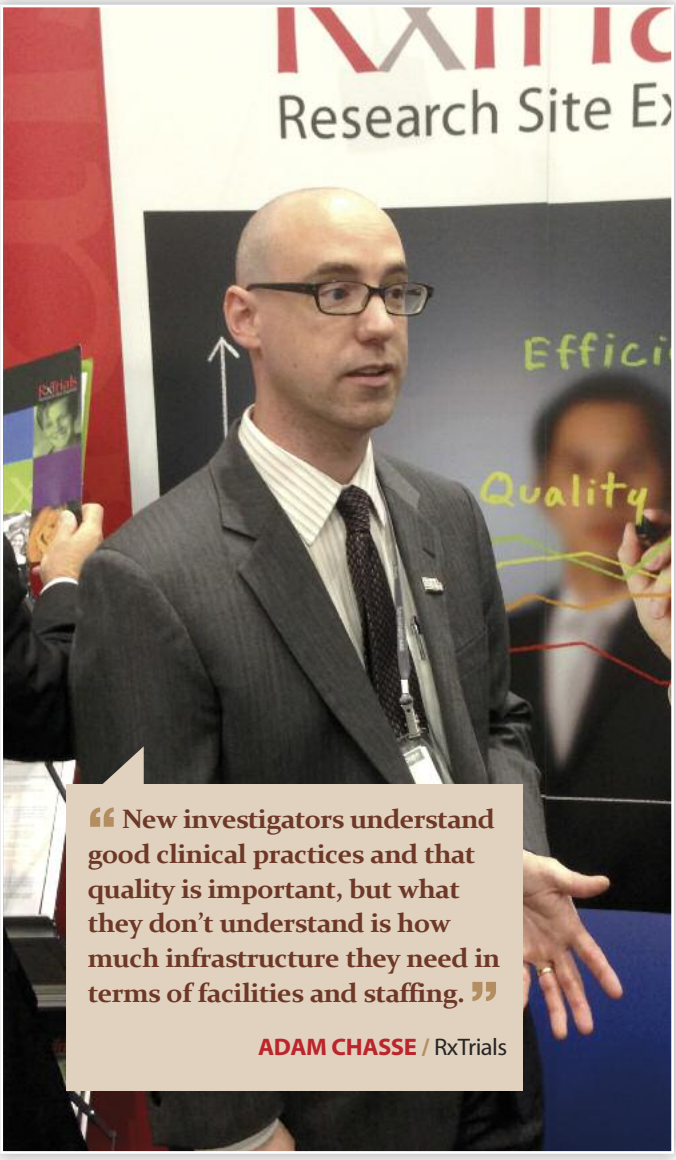
As a result, according to CenterWatch, as experienced investigators find it harder to stay in clinical research, the investigator market is more fragmented, with newer investigators and investigators who only conduct one study a year.

"Without a stable environment for investigators to operate within, our industry is going to be built on a very fragile foundation," says Christine Pierre, president of the Society for Clinical Research Sites.

Why Investigators Leave

Ms. Pierre says her organization conducted a survey last year at the Site Solutions Summit asking participants if they knew of sites that had closed their doors in the previous 18 months. About half knew of an investigative site that had.

"I gets calls from sites and investigators who are going out of business; the primary reason they cite is the extensive amount of work required of them for reimbursement," she says. "Another reason we hear is the tremendous amount of regulatory rigor that is expected in clinical research versus in clinical practice. The reality is that it takes time — not just didactic training — and actual experience doing clinical research before the investigator or coordinator understands the amount of documentation that is required to



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> **ADAM CHASSE** / RxTrials

FAST FACT

ALMOST 28,000 PRINCIPAL INVESTIGATORS AROUND THE WORLD PARTICIPATED IN CLINICAL STUDIES IN 2012, WITH 61% OF THEM BASED IN NORTH AMERICA, DOWN FROM 84% IN 1996.

Source: Tufts CSDD

substantiate the expectations of the FDA, the sponsor, and the protocol."

Adam Chasse, chief operating officer at RxTrials, says there is a learning curve for new investigators.

"They understand good clinical practices and they understand that quality is important, but what they don't understand is how much infrastructure they need in terms of facilities and staffing," he says. "They don't appreciate until they get into their first protocol how complex protocols tend to be. They may agree to a budget for a study and not realize where the hidden costs are."

Industry experts say substandard budgets and payment terms are two challenging aspects for investigators. Mr. Chasse says pharma companies tend to have payment terms in their contracts that are not small-business friendly.

"Additionally, the volume of work must be steady enough to justify the infrastructure for investigators, otherwise they're always operating on a shoestring," he says.

Roger Smith, senior VP of operations at Acurian, says pharma companies treat investigators the way they do larger, established providers of services.

"Investigators who work with big pharmaceutical companies often have to float cash for 90 or 120 days and that is a real burden for a small business, especially when that investigator is offering a service that companies say they highly value," he says.

Mr. Smith says the clinical study marketplace is becoming less and less lucrative especially for physicians who want to do a few studies a year.

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> **ROGER SMITH** / Acurian

"Pharma companies don't have a great reputation for fixing holes in their processes unless they have to or are forced to," he says. "It probably is going to take a shortage of investigators to make them holistically address their payment practices, not only rates but also float terms and speed at which payment turns around and other services that would make being an investigator a more attractive proposition."

These comments echo the CenterWatch study, which found that even experienced investigators are leaving research because of practices implemented by drug sponsors over the last decade.

Increasingly complex protocols, flat study budgets, more demanding workloads and competition for studies with inexperienced investigators who accept unrealistic contracts have forced some veteran investigators out of business.

Motivating Investigators

Ms. Pierre says according to the survey conducted at 2012 Site Solutions Summit, 127 site respondents reported they knew of sites that had closed their doors in the previous 18 months.

When asked why, they cited: inadequate compensation, 31%; lack of study opportunities, 30%; slow payment terms, 15%; too much regulatory burden, 8%.

Ms. Pierre says in the past few years many of these sites closing their doors are not the typically "one and done" study sites.

"These are reputable sites that have been long-standing contributors to our industry," she says. "There is a clear message here that industry can embrace and react to in a favorable way by assisting sites in maintaining their commitment to being a research site. Sponsors need to work with sites to establish what is true fair market value as opposed to using data from prior study budgets where sites agreed to compensation that did not reflect what their true costs were and agree to pay sites on a monthly basis."

Mr. Smith also suggests companies provide a set of support services to investigators.

"A doctor, especially if he or she is only doing a couple of studies a year, may not want to take on the expense of a full-time recruiter or study coordinator," he says. "Pharma companies could offer a set of services to lessen the negative impact on a physician's practice." PV