

Insider Insights:

Pamela Tenaerts, M.D., Clinical Trials Transformation Initiative (CTTI)

CWWeekly's semi-monthly company profile feature, *Insider Insights*, interviews executives of companies and organizations in the clinical trials space. Staff Writer Ronald Rosenberg sat down with Pamela Tenaerts, M.D., executive director of the Clinical Trials Transformation Initiative.



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Q Since its formation in late 2007, as a public-private partnership co-founded by the FDA and Duke University, how has CTTI evolved from its mission to identify practices that will increase quality and efficiency of clinical trials? What are some of its biggest successes and disappointments?

A When CTTI originated in 2007, our mission statement was to identify practices that would increase the quality and efficiency of clinical trials. In January 2013, we updated that mission to include the promotion of practices that increase the quality and efficiency of clinical trials. This change stemmed from our members, who felt creating recommendations was valuable, but additional tools and work were needed to ensure others could implement the changes we were recommending.

With this change in mission, we also updated our methodology. Previously, we would identify a topic, collect evidence on the relevant issues

and then develop recommendations to improve clinical research. Now, once the recommendations are developed, we create a follow-up project that is either an implementation or a demonstration project. We ask, what are the

tools people need and how can we show examples of how this change can happen so others can emulate it? Our project teams work to provide these tools and examples. This expansion was important for our members, because they recognized culture change is difficult, and providing recommendations is not always enough to convince people that changing practices is both worthwhile and possible.

Another change is the greater inclusion of patients in our processes. We have always had two patient

representatives on our steering committee and one on our executive committee. In 2012, we started talking to patient advocacy groups about how they could be more a part of what we do. We felt patients were not always looked upon as equal partners in improving the clinical trial enterprise, so we created a patient leadership council that included 17 thought leaders from patient advocacy groups.

From that patient leadership council, we created a project looking at patient groups in

Year founded: 2007

Headquarters: At the Duke Transformational Medicine Institute of Duke University School of Medicine, Durham, N.C.

Description: A membership organization established by the FDA and Duke as a public-private partnership to identify and promote practices to increase the quality and efficiency of clinical trials. It conducts a range of projects to improve current practices, evaluate alternative approaches, understand barrier to change and propose recommendations for improvement. It disseminates recommendations and encourages system changes to improve efficiency in clinical trials. A key goal is to develop evidence-based work to inform both policy and decision-making in the interest of public health and streamline trial operations.

Officers: Pamela Tenaerts, M.D., executive director
Leanne Madre, JD, director of strategy
Bray Patrick-Lake, director of stakeholder engagement
Matthew Harker, associate director of projects

Employees: 15

Projects: 8 since 2007; 4 more due for completion in first half of 2015

Members: 70 including representatives from: government agencies such as the FDA, NIH and Dept. of Veterans Affairs; pharma, biotech and medical device companies; CROs; patient advocacy groups; academic institutions; and investigative site groups.

Web site: www.ctti-clinicaltrials.com

clinical trials. A goal was to identify best practices for engaging with patients to improve clinical trials. We found there are currently not any best practices—there are varying types of patient engagement with no evidence of what works best and the actual impact or value, so we have taken on this effort.

One of our biggest successes is a forum we created, in which there is trust for open dialogue. When people come to our meetings, they can say what they think with other people in the room. That open communication and honesty is really what you need to identify the barriers to doing things differently, including more efficiently and more quality driven. This atmosphere allows us to



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have all the stakeholders in clinical trials involved in being part of the solutions.

A disappointment is that we are not going faster than we are now. There always is a sense of urgency, and everyone is very passionate; with passion comes urgency.

Q What are the key recommendations for streamlining Good Clinical Practice (GCP) that will reduce redundant training yet update the content and frequency?

A Compliance with GCP is intended to assure the rights, integrity and confidentiality of clinical trial participants are protected. What we found is that investigators have to do GCP training repeatedly at the start of every clinical trial. There is a perception that time is lost and that energy could be spent on other activities rather than repeating GCP training over and over again.

We have identified 13 elements that are the minimal essentials for GCP training, and they are the same as the investigators' section of International Conference on Harmonization (ICH) GCP guidance. Other things may be considered as needed, depending on the nature and scope of the research. Training should focus on aspects outside of normal medical practice and those in recurring non-compliance of GCP.

We are recommending a minimum training frequency of every three years. The training should be mutually accepted across organizations, so training completed at one company would be acceptable to another company within the three-year timeframe. We also felt the training should be done with a purpose. We don't have recommendations on format, but online training seems to make sense in many cases. Finally, ensuring people satisfactorily completed the program does not necessarily require a test. Instead of an exam, it could be a certificate or some other formal confirmation.

Q In recommending greater use of central IRBs to improve the quality and efficiency of multicenter clinical trials, what prompted the development of a guide—the Considerations

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Clinical Trials Transformation Initiative

Document—to support communications and contractual relationships between member institutions and a central IRB?

A We started off by identifying the barriers to using a central IRB, because both the FDA and the Office for Human Research Protections (OHRP) indicated they were in favor of central IRBs, but we saw a lot of institutions were not using them. We interviewed IRB administrators at various institutions to figure out why they were not allowing use of a central IRB for multi-center studies. This also is known as a single IRB of record.

We found a lot of institutions were confusing institutional responsibilities with regular IRB responsibilities. For a multi-center study that would use a single IRB of record, the question would then arise of who would take on the institutional responsibilities. The Considerations Document attempts to delineate what the institution is responsible for, what the IRB typically needs to address and a third category in which either entity could assume responsibility. This division of responsibilities should create clarity when an institution is faced with the opportunity to rely on a single IRB of record.

Q Explain CTTI's push for periodic evaluation of the totality of safety information during the drug or biological development program, rather than conducting such analyses at the time of NDA or BLA submission?

A That is not a CTTI recommendation. The FDA has a guidance on reporting requirements for serious and unexpected events during clinical trials. In clinical trials, you have to make sure your participants are being kept safe, while at the same time collecting information about your drug for your NDA or BLA submission.

When we first started this project, it was before the new FDA guidance came out. Back then, any serious adverse events for a particular drug were sent to all investigators involved in clinical trials with that drug. Investigators were getting inundated with IND safety reports every week, and it was difficult for them to make sense of what was a trend or important and what wasn't.

We found compliance with the guidance is not always optimal, and we are now doing a follow-up project in oncology, where serious adverse events are prevalent, to help figure out how best to comply. It's a matter of having an ongoing idea of the safety profile of your drug while you are doing the research.

Q Given the range of CTTI projects, how important is greater development of open sharing of clinical trial data that not only protects patients, but also provides and expands the availability of completed trial information to a broad audience?

A The big data question is something we haven't necessarily tackled in a CTTI project. It has come up particularly around the quality by design project. To have a good scientific question, you need to know what other people have done. If clinical trial data are not made publicly available, people can't learn from other trials to design their next trial.

The fact that the knowledge is omitted from the public domain creates a situation in which the next trials cannot live up to their potential. In my opinion, clinical trial data sharing will allow everyone to learn from what has happened, whether the trial result is negative or positive. 