Over the past decade, CTTI has helped to make important strides in modernizing the clinical trials enterprise to be more streamlined, efficient, and patient-centered.”

- Scott Gottlieb, MD, Commissioner, U.S. Food and Drug Administration
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Judith Kramer, MD, MS
CTTI Executive Director | 2007-2012

WHY WAS CTTI CREATED, AND WHAT WAS MOST EXCITING WHEN CTTI BEGAN?
In 2007, with a growing need for evidence-based answers to therapeutic questions, clinical trials had become too expensive and inefficient to fulfill the need. In response, Duke University and the U.S. Food and Drug Administration (FDA) worked together to found a multi-stakeholder organization dedicated to improving clinical trials. It was exciting to witness the eagerness to participate in this effort from such a broad array of disciplines.

WHAT CHALLENGES DID CTTI FACE STARTING OUT?
Operationalizing the vision for CTTI was a huge undertaking. Figuring out the methods that would allow us to gather reliable information to make trials more efficient did not happen overnight. Project by project, we involved experts and evolved our methodology to what it is today.

WHAT DO YOU SEE AS CTTI’S GREATEST ACCOMPLISHMENT?
CTTI being a truly collaborative effort is its greatest accomplishment. This can be seen in the continued positive and constructive interactions between industry, academia, regulatory agencies, and patient advocates to solve problems for the good of patients and not out of self-interest. The longevity of CTTI and continued commitment of those who volunteer their time is heartening.

ONE DECADE OF IMPACT...
Interview with
Pamela Tenaerts, MD, MBA
CTTI Executive Director | 2012-Present

WHAT IS YOUR BIGGEST ACHIEVEMENT AT CTTI AND WHAT ARE YOU MOST EXCITED FOR, FOR THE FUTURE?

At CTTI, we can be most proud of our robust portfolio of evidence-based recommendations and resources, which have helped to inform shifts in policy and fueled improvements across the clinical trials enterprise. Our Quality by Design work is creating a movement to build quality into clinical trials upfront, and including all stakeholders—especially patients—as equal partners in designing clinical trials is leading to higher quality, more efficient trials. Looking to the future, we can continue to accelerate progress in clinical trials by questioning the status quo and working with all stakeholders to innovate.

HOW IS CTTI EVOLVING TO MEET THE NEEDS OF CLINICAL RESEARCH STAKEHOLDERS?

Since project topics are prioritized by our members, we know we are tackling issues that matter. CTTI is also becoming more proactive in helping to drive adoption of our recommendations and resources to create an environment where transformation is closer than ever.

WHAT WILL CTTI HAVE ACCOMPLISHED 10 YEARS FROM NOW?

When we look back in 10 years, we will see how CTTI has shaped thinking, policy, and practices to enable streamlined, patient-centric clinical trials that provide answers to questions that matter. Patients will have benefited from these improvements, and more diseases will have evidence-based treatments.

...ONE VISION AHEAD
Transformation in Action

CTTI’s work over the past 10 years has dramatically changed how organizations think about and conduct clinical trials, and has shaped major policy decisions regarding clinical research.

Two key examples of CTTI’s transformational influence are in promoting patient engagement and clinical trial quality.

OUR WORK CONTINUES TO ADVANCE THE FIELD AND HAVE LASTING IMPACT.

Advancing Trial Quality

CTTI supported a paradigm shift in clinical trial quality. We developed the Quality by Design concept and helped make it common practice for clinical trials—taking the focus from a reactive approach using audits and monitoring, to a proactive approach that builds quality into clinical trials starting with protocol development. These strategies reduce the burden of trial conduct and improve efficiency. CTTI’s Quality by Design recommendations remain our most downloaded, and this work has been cited by FDA and EMA guidance and incorporated into GCP guidelines.

In the past 10 years, individuals from >430 organizations have been involved in CTTI project teams or meetings.
Since 2007, CTTI has been at the forefront of transforming the clinical trials enterprise, developing recommendations and resources that can improve the efficiency and quality of clinical trials.

**OUR UNIQUE STRENGTHS ARE THAT WE:**

► Engage all stakeholders equally, bringing together diverse viewpoints to improve clinical trials.

► Use an evidence-based approach to address the breadth of challenges to quality, efficient clinical trials.

► Are committed to driving adoption of improved practices by providing resources and support to the clinical trials community in making these changes.

CTTI has provided a valuable platform for regulators, clinical trial sponsors, and patient advocates to challenge the status quo and build consensus on what really matters to support good decision-making on medicines and, in turn, empower patients to make good decisions about their own healthcare.”

– Fergus Sweeney, PhD, Head of Inspections, Human Medicines Pharmacovigilance and Committees, European Medicines Agency
CTTI in 2017

5 NEW SETS OF NOVEL, EVIDENCE-BASED RECOMMENDATIONS:

► Developing Novel Endpoints Generated by Mobile Technologies for Use in Clinical Trials

► Making Registries Into Reusable Platforms for Conducting Clinical Trials

► Strengthening the Investigator Site Community

► Planning for Pregnancy Testing in Clinical Trials

► Improving Pediatric Trials in Antibacterial Drug Development

“

We are shaping the future of clinical research by delivering recommendations that empower stakeholders across the enterprise to improve today’s clinical trials.”

– Mark B. McClellan, MD, PhD, CTTI Executive Committee Chair
Removing Barriers to the Adoption of Mobile Technologies in Clinical Trials

Mobile technologies offer the potential to increase the quality and efficiency of clinical trials. Potential benefits include expanded patient recruitment, improved patient experience, continuous high-quality data acquisition, and reduced costs.

With our Mobile Clinical Trials (MCT) Program, CTTI is identifying and addressing challenges related to planning for and conducting clinical trials that use mobile technologies. Four CTTI projects each target a specific challenge that could threaten or delay widespread adoption of these promising technologies in clinical research.

We surveyed potential research participants and conducted in-depth interviews with site investigators to develop recommendations that will ensure their needs and concerns are addressed. We also held expert meetings to refine solutions to scientific and technological issues and to characterize actual and perceived challenges to conducting decentralized clinical trials in the U.S. The findings are being used to develop recommendations and resources to guide the adoption of mobile technologies for data capture in clinical trials.

PATIENT VIEWS ON MOBILE TECHNOLOGIES IN CLINICAL TRIALS

- **76%** would prefer to participate in a mobile trial vs. a traditional trial
- **90%** said they are willing to use alternate forms of communication with a trial doctor (other than in-person visits)
- **100%** reported that it’s important for wearable monitors to be easy to learn and convenient to use

*Source: CTTI survey of potential trial participants in 2017*
Generating Novel, Tech-Derived Endpoints for Clinical Trials

CTTI released recommendations for using mobile technologies to generate novel endpoints for clinical trials. This approach provides new ways to capture objective measurements as clinical trial participants go about their daily lives, offering the opportunity to reduce barriers to participation and provide high-quality data pertaining to outcomes that are meaningful to participants.

**BETTER RESOURCES = BETTER TRIALS**

In addition to the recommendations, CTTI produced a number of resources to assist with selecting and developing viable novel endpoints, including an interactive selection tool, a flowchart of steps for novel endpoint development, and a quick reference guide. We also provided several case studies of mobile technologies being used to develop novel endpoints.

As we embark on a two-phase effort to develop a digital battery for use in Huntington disease trials, we plan to use CTTI’s MCT Novel Endpoints recommendations to guide our work. In doing so, we feel strongly that we can reach our goal more quickly and more efficiently—ultimately, and most importantly, benefiting patients.”

– Valentina Dilda, PhD, Director, Experimental Medicine, CHDI Foundation

**CASE STUDY**

A collaboration between monARC Bionetworks and the Pulmonary Fibrosis Foundation is planning to develop a digital measure of forced lung volume in the home for use in idiopathic pulmonary fibrosis clinical trials and is using the MCT Novel Endpoints recommendations to inform their work.
Drawing on Real World Evidence for Better Evaluation of Medical Products

When incorporated into randomized clinical trials, “real world evidence” (RWE)—the clinical evidence derived from analysis of real world data (RWD)—may provide insights into important scientific or clinical questions that would otherwise be impossible to answer. RWE may also help create a more accurate picture of patient experiences while making clinical trials more streamlined and efficient. Despite the considerable benefits, lack of consensus among stakeholders about appropriate approaches for using RWD and RWE to support regulatory submissions has slowed progress. CTTI is helping to pave the way with a new project on appropriate use of RWD and RWE in randomized controlled trials, as well as recently released recommendations on registries as reusable platforms for clinical trials.

USING REGISTRIES FOR MORE EFFICIENT CLINICAL TRIALS

Although registries are typically used to better understand long-term trends in a specific population, they can also be used as a data source for clinical trials if designed appropriately. CTTI’s recommendations for using registries in clinical trials outline best practices for assessing and designing registries so that the data can meet expectations for FDA review of new products. These best practices include ensuring data are sufficiently reliable and robust, putting in place adequate measures for patient protections and data confidentiality, and incorporating processes for auditing, documentation of informed consent, and randomization.

“High-quality registries are an increasingly important source of evidence for regulatory decisions and surveillance, conveying important information, for example, regarding real world medical product use and outcomes throughout the total product life cycle.”

– John Laschinger, MD, Medical Officer, U.S. Food and Drug Administration

BETTER RESOURCES = BETTER TRIALS

CTTI’s recommendations include decision trees to aid in the assessment of existing registries for use in clinical trials, as well as detailed requirements for designing new registries capable of informing regulatory decision-making.
Strengthening the Investigator Community

Clinical investigators are critical for trial success, yet many do not conduct another trial after their initial study. CTTI investigated the reasons for high investigator turnover, surveying over 200 investigators.

The evidence suggests that many investigators leave due to difficulty balancing workload, time requirements to conduct trials, data and safety reporting burdens, and financial issues. However, investigators value the professional and personal rewards of conducting clinical research and are willing to work to overcome these challenges. Of “one and done” investigators, 44% were interested in conducting another trial if they could be connected with opportunities.

The recommendations outline actions tailored for different stakeholders—investigators, sponsors, contract research organizations, and health systems—as well as cross-cutting strategies to create a research environment that sustains long-term engagement.

CASE STUDY

IQVIA is putting CTTI’s recommendations into practice to promote a more welcoming and sustaining environment for investigators. Recognizing the importance of acknowledging investigators and sites for their efforts, it is examining ways to improve its existing site recognition program. It is also addressing burdens related to trial conduct by streamlining processes and communications with sites, prioritizing the inclusion of patient and site perspectives in protocol development from the earliest stages, and strengthening research infrastructure through its site management organization.
Promoting Inclusion of Women in Safer, More Efficient Trials

There is broad agreement on the importance of including women in clinical trials. However, there are no specific guidelines for how pregnancy testing should be conducted to prevent the unintended exposure of an embryo or fetus to a study’s intervention, nor how risks should be clearly communicated to women.

Creating pregnancy testing plans can support the inclusion of women in research and lead to safer, more efficient trials. CTTI developed recommendations, along with an interactive web application, to provide investigators, sponsors, IRBs, and others a standard way to plan for and make decisions about pregnancy testing by assessing the balance of benefits and burdens of different pregnancy testing plans. They also include specific recommendations for the informed consent process to improve communication and transparency with trial participants.

“This work is another important step in promoting the inclusion of women in research and encouraging transparent communication with trial participants.”

– Veronica L. Todaro, MPH, Senior Vice President, Chief Operating Officer, Parkinson’s Foundation

Better Resources = Better Trials

The Pregnancy Testing Outcomes Predictor for Clinical Trials is an easy-to-use interactive tool to help investigators, sponsors, regulators, and others in designing a pregnancy testing plan for a clinical trial by estimating the likelihood of a woman enrolling in the study while pregnant or becoming pregnant during the study. By calculating the probability of pregnant participants, the tool provides a quantitative method to assess the advantages versus burdens of a pregnancy testing plan.
Improving Pediatric Trials

Part of CTTI’s Antibacterial Drug Development (ABDD) Program focused on making antibacterial trials more efficient and less burdensome for pediatric patients and their families—work that can also extend to other therapeutic areas.

Pediatric trials—while critically needed to inform dosing, efficacy, and safety of treatments in children—are especially difficult to design, enroll, and complete, particularly in populations with antibacterial infections. The time from approval of a new antibacterial drug for use in adults to pediatric labeling can be five years or longer.

CTTI worked to identify the difficulties with conducting pediatric antibacterial trials and issued recommendations to address the unique challenges. Our recommendations offer practical, evidence-based strategies to improve the quality and efficiency of pediatric antibacterial trials, including methods for streamlining trial design, approaches for improving the informed consent process, and special considerations for conducting trials with neonates.

This work matters to the lives of families like mine.”
– Breck Gamel, parent participant in the CTTI effort

80% OF CLINICIANS IDENTIFIED PARENT CONCERNS TO BE A BARRIER FOR COMPLETING RESEARCH, EMPHASIZING THE NEED FOR BETTER ENGAGEMENT.

These recommendations encourage consultation with the FDA on pediatric study plans early in drug development and emphasize the potential utility of global study networks and streamlining trials. Our mutual goal is to provide data in the drug labeling that will better inform the safe and effective use of antibacterial drugs in children.”
– Sumathi Nambiar, MD, MPH, Director, Division of Anti-Infective Products, U.S. Food and Drug Administration
Growing Impact & Awareness in 2017

92% of CTTI members report that CTTI has had an impact on the way clinical trials are developed at their organization*

100% of CTTI members feel CTTI has had an impact on the U.S. clinical trials enterprise*

26,000+ web downloads of CTTI recommendations & resources

12 CTTI-authored articles published

63 presentations given at professional conferences & webinars

1,100+ citations of CTTI publications through 2017

"CTTI has been enormously successful in bringing together stakeholders, asking difficult questions, rigorously exploring new solutions, and crafting recommendations that go beyond ‘making sense’ and are instead evidence-based. I am optimistic that we will continue to raise the clinical trial enterprise to higher levels of success.”

– Michael Lauer, MD, Deputy Director for Extramural Research, National Institutes of Health

*Data from CTTI members who completed the 2017 member survey.
On the Horizon

Our work is continually evolving to meet the needs of the clinical trials enterprise. Through FDA and membership input, we make sure to address the latest trends, top barriers, and leading opportunities in clinical research. We have a host of exciting efforts underway—stay tuned for more CTTI resources to help you transform your clinical trials.

FORTHCOMING RECOMMENDATIONS

► Effective qualification of investigators to conduct quality clinical trials
► Scientific and technological barriers to the use of mobile technologies in clinical trials
► Legal, regulatory, and practical considerations affecting the adoption of decentralized clinical trials
► Barriers to the use of mobile technologies in clinical trials as perceived by key stakeholders, including site investigators and potential research participants

COLLABORATIVE EFFORTS

A collaboration is ongoing to investigate conducting the first clinical trial using Sentinel.

CTTI will host the Patient Engagement Collaborative—a forum for the patient community to exchange ideas with FDA about increasing patient engagement in regulatory discussions about medical products.

CTTI’s work to drive adoption of these recommendations has been extremely important in changing perceptions and practice. As we move from answering why patients should be engaged to how to engage effectively, CTTI’s new partnership with FDA to convene the Patient Engagement Collaborative will be a key forum for actionable solutions.”

Kimberly McCleary, Senior Advisor, FasterCures
A Foundation for the Future

Over the past 10 years, CTTI has influenced many facets of the clinical trials enterprise. We have created profound shifts in thinking to bring about quality, efficient, and patient-focused clinical trials. Our work has been cited by FDA, EMA, NIH, and other policymaking organizations, and our resources are used every day by sponsors, investigators, research professionals, patient groups, and others.

We completed more than 25 projects since 2007, and we continue to tackle prominent issues that can advance the field. Several of our latest projects draw on recent advances in technology and data sciences to bring about improvements for clinical trials. CTTI will play a key role in ensuring that these advances are integrated in a way that maintains or enhances trial quality and efficiency.

In the years ahead, we will elevate our efforts to drive adoption of improved practices, share successful implementation case studies with the CTTI community, and use a new framework to measure our impact on the clinical trials enterprise.

THANK YOU FOR BEING ON THIS JOURNEY WITH US. WE CAN’T WAIT FOR YOU TO SEE WHAT’S NEXT IN OUR QUEST TO TRANSFORM CLINICAL TRIALS.
Thank You

We would like to thank all of our members for their contributions toward improving the clinical trials enterprise. CTTI members generously dedicate their time and expertise to develop solutions that can be used by the wider research community, and they often serve as early adopters of improved practices.

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AdvaMed
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Alliance for Lupus Research
Alnylam Pharmaceuticals
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*Served on the Executive Committee for part of 2017