

One Decade of Impact. One Vision Ahead. Optimizing the Power of Public-Private Partnership: Lessons Learned from the Clinical Trials Transformation Initiative

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Background

CTTI was co-founded by the U.S. Food and Drug Administration and Duke University to improve efficiency and quality in clinical trials. CTTI now comprises a diverse membership reflecting the range of organizations involved in the design, conduct, and evaluation of clinical trials, and engages a vast array of stakeholders in its work.¹ Our approach to stakeholder engagement is much broader than membership, with individuals from more than 430 organizations having been involved in CTTI project teams or meetings. CTTI's mission is to develop and drive adoption of practices that will increase the quality and efficiency of clinical trials. Through a series of projects and collaborative efforts, CTTI offers solutions for significant improvements or advancements in clinical trials to stakeholders in the clinical trials enterprise (CTE) (Figure 1).

Figure 1. CTTI project portfolio

Areas of Strategic Focus:	SYSTEMATIC EVIDENCE GENERATION	PATIENTS AS EQUAL PARTNERS	EFFICIENT & QUALITY TRIALS	PUBLIC HEALTH CONCERN	SAFE & ETHICAL TRIALS
Active Projects:	MCT Legal & Regulatory MCT Mobile Devices MCT Stakeholder Perceptions Real World Evidence State of Clinical Trials	Patient Groups & Clinical Trials	Investigator Qualification	ABDD HARP/VABP Studies	
Complete Projects:	Large Simple Trials MCT Novel Endpoints Registry Trials		GCP Training Investigator Community Monitoring Quality by Design Recruitment Site Metrics	ABDD Peds Trials ABDD Streamlining HARP/VABP Trials ABDD Unmet Need Long-Term Opioid Data	Central IRB, Central IRB Adv DMCs Informed Consent Pregnancy Testing IND Safety, IND Safety Adv SAE Reporting

Pursuit of Efficient and Quality Clinical Trials

CTTI has conducted more than 25 projects within 5 strategic focus areas¹ and issued recommendations for specific actions and considerations to improve the design and execution of clinical trials,¹ with a goal of assuring meaningful, high quality data and appropriate protections for participants (Figure 2).

Results and recommendations have been cited by government bodies and are being implemented by sponsors, academic organizations, patient advocacy groups, and others (Figure 3).

Figure 2. Summary of CTTI recommendations

RECOMMENDATIONS & TOOLS

CTTI has issued more than 30 sets of evidence-based recommendations, frameworks, and tools to make better clinical trials a reality:

- Apply **Quality by Design** principles to create better protocols
- Involve **Patient Groups** as equal partners
- Move **Recruitment** planning upstream to reduce barriers to participation
- Perform higher quality **Informed Consent** process
- Improve ethics review process via use of **Central IRB**
- Reduce inefficiencies of investigator **GCP Training**
- Organize **DMCs** to ensure patients' safety
- Develop a better **IND Safety Reporting** system
- Create **Pregnancy Testing** plans for improved clinical trials
- Use **Registries** to conduct more efficient clinical trials
- Identify the best pathways for developing **Novel Endpoints** generated by mobile technologies
- Streamline **Antibacterial Pediatric and HARP/VABP Trials**
- Strengthening the **Site Investigator Community**

Figure 3. CTTI's strategic areas of focus — highlighted project results

Strategic Area	Highlighted Project Results
Systematic Evidence Generation	<ul style="list-style-type: none"> Suggested best practices for determining if a registry is appropriate for embedding clinical trials Released recommendations to help stakeholders develop novel endpoints based on data from mobile technologies for use in regulatory clinical trials Facilitated 7,315 downloads of the Aggregate Analysis of ClinicalTrials.gov (AACT) datasets in 2017, which provide important insights on the state of clinical trials
Patients as Equal Partners	<ul style="list-style-type: none"> Facilitating a culture change to increase meaningful engagement with patient groups in clinical trials through the Patient Group & Clinical Trials project and CTTI's own engagement with the patient/caregiver community Partnering with the FDA to create a forum for discussing how to better engage patients in regulatory discussions across the FDA Implemented a policy to compensate patient representatives for their work on CTTI projects
Efficient & Quality Trials	<ul style="list-style-type: none"> Developed an innovative approach that organizations can apply to move strategic recruitment planning earlier, increasing recruitment success and alleviating downstream challenges Offered practical solutions to address the administrative, financial, and logistical burdens that are causing investigators to abandon clinical research Facilitated >1,000 downloads of our Quality by Design recommendations, which sponsors apply to improve trial integrity and efficiency
Public Health Concerns	<ul style="list-style-type: none"> Developed principles for more feasible and streamlined hospital-acquired and ventilator-associated bacterial pneumonia (HABP/VABP) trials Conducting risk factor study to provide evidence that following these patients may lead to possible recruitment in clinical trials, thereby supporting organizations in adopting our early enrollment strategy for more feasible HABP/VABP trials Released evidence regarding patient and physician perspectives on the use of streamlined antibacterial drug development approaches to inform future use of these approaches
Safe & Ethical Trials	<ul style="list-style-type: none"> Facilitated adoption of a single IRB of record through release of recommendations, resources, and providing examples of success Issued recommendations to help sponsors increase their adherence to FDA requirements for IND safety reporting Published recommendations for data monitoring committee (DMC) organization & conduct to enhance the quality of trial oversight

Lessons Learned: Successes and Challenges

PROJECT SELECTION

Targeting the collective needs and priorities of industry, academia, clinical trial sites, patients, and government bodies is fundamental to project success, and optimal adoption of the project recommendations occurs when the project results address the needs of relevant stakeholders.

CTTI has fine-tuned its selection of projects to ensure key questions are considered upfront; examples include anticipated impact, criticality of issue, potential for transformation, regulatory needs, relationship to CTTI's current or past projects, and relationship to efforts of other organizations.

PROJECT TEAM DYNAMICS AND EXECUTION

Enlisting knowledgeable, engaged, committed project leaders and team members representing diverse perspectives is crucial throughout the duration of the project. With a typical project spanning approximately 2 years, multi-stakeholder teams collaborate on all project activities, from gathering evidence related to the topic of interest, to formulating project recommendations and associated resources.

MULTI-STAKEHOLDER MEETINGS AND DISCUSSIONS

CTTI strives to engage multi-stakeholder groups from project inception through project execution and beyond. CTTI has witnessed tremendous value in team discussions that lead to moments of common understanding between diverse stakeholders. These discussions are expanded during expert meetings designed to engage the wider trials community and allow issues to be explored further, solutions to be identified, and additional work can be determined.

REFERENCES:

- Clinical Trials Transformative Initiative. <https://www.ctti-clinicaltrials.org>.
- Landray MJ, Grandinetti C, Kramer JM, Morrison BW, Ball L and Sherman RE. Clinical Trials: Rethinking How We Ensure Quality. *Drug Information Journal*. 2012; 46: 657-60.

Common Themes Identified in CTTI Projects and Recommendations

IMPORTANCE OF ENGAGING MANY STAKEHOLDERS

One of CTTI's core principles is to value the input and participation of all stakeholders, and we encourage others to do the same in nearly every set of project recommendations.

ADVANCED PLANNING TO ADDRESS CRITICAL ISSUES

Many problems that may occur during a clinical trial can be prevented or mitigated through effective, proactive thought and planning.² CTTI's Quality by Design (QbD) project developed a new approach to build quality into the scientific and operational design of the clinical trial in a prospective and ongoing fashion. This is accomplished by focusing on activities that are critical to ensure the credibility of study results and ensure the safety of trial participants,¹ engaging a broad range of stakeholders in trial planning, creating a culture that values critical thinking, as well as prospectively identifying and periodically checking critical to quality factors.¹

DISCONTINUE NON-VALUE ADDED PRACTICES

Recommendations from many projects suggest specific opportunities to focus on critical data and activities, with strategies to avoid activities that are not essential. As noted above, the QbD process asks us to consider whether nonessential activities may be eliminated from the study to simplify conduct, improve trial efficiency, and allocate resources to the most critical areas. Another example are the recommendations of the GCP projects where sponsors are encouraged to only retrain investigators every 3 years and accept other sponsors training under certain circumstances. You will find many recommendations that carry thru on that theme such as embedded in CTTI's ABDD program and safety reporting projects.

TECHNOLOGY PRESENTS NEW OPPORTUNITIES

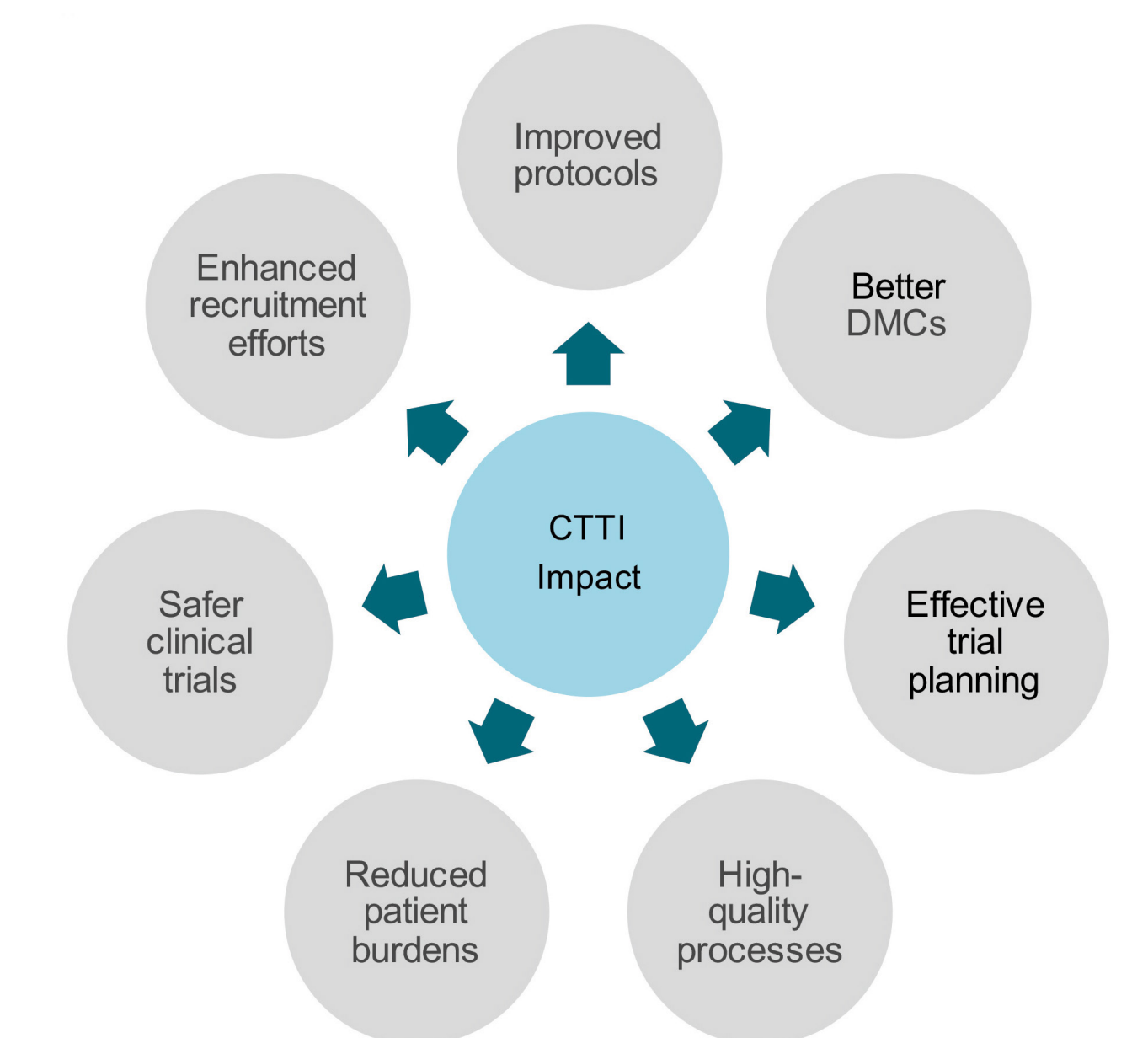
Advances in novel technologies and increasing access to health data, such as electronic health records (EHR) provide opportunities to increase the efficiency of many clinical trials and to improve the quality of the information that they provide. CTTI is working with many stakeholders to understand how we can take advantage of technology, while making sure that the results are reliable, and participant protections remain robust. CTTI's Mobile Clinical Trials (MCT) program focuses on reducing barriers to the incorporation of mobile technology in FDA-regulated clinical trials.¹ Other CTTI projects are exploring the application of existing data sources, such as the FDA Sentinel System,¹ registries and EHR systems for clinical trials.

Impact to Date and a Look to the Future

While there is more work to be done to truly transform clinical trials, much has been accomplished in the past 10 years, and CTTI has made a difference (Figure 4).

No effort is without its challenges, but as CTTI celebrates 10 years of successfully driving change in the CTE, we are committed to efforts that question the status quo and work with all stakeholders to make clinical trials more efficient, quality-driven, and patient-focused.

Figure 4. CTTI's impact on the clinical trials enterprise



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