Master Protocol Studies: Emerging Best Practices to Drive Multi-Stakeholder Collaboration & Mobilization

Master protocols studies have the potential to more efficiently ask and answer scientific questions–ultimately, getting the right drugs to patients more quickly. Particularly in light of COVID-19, interest in master protocols in diseases other than oncology or COVID-19 infections is growing – but many organizations lack experience in running master protocol studies, presenting major study design and operational challenges.

Starting in the summer of 2019, CTTI convened experts and key stakeholders across the clinical trials ecosystem to develop publicly available resources that address these challenges. These new tools help sponsors, non-profit groups, and others to appropriately use master protocols in diverse therapeutic areas.

Additionally, based on a thorough landscape analysis and several discussions with stakeholders who have run, or are running, a master protocol study, CTTI has identified four emerging best practices for driving multi-stakeholder collaboration and mobilization during a master protocol study.

CTTI Master Protocol Resources

- FDA Engagement Tool
- High-Level Roadmap
- Master Protocol Content Development Guide
- Master Protocol References & Resources
- Operational Partner Assessment Tool
- Statistical Simulation Tool
- Study Execution Case Studies
  - ALCHEMIST
  - STAMPEDE
- Value Proposition Guide

1. Facilitate early, meaningful, and consistent engagement with patient communities across all stages of study design and conduct.

A key success factor in running a master protocol study, will be early and frequent engagement with patients and patient groups to discuss and collaborate on study features such as eligibility criteria, lower screen failure rate, and approaches for greater patient centricity and accessibility.

Related CTTI tool:

- Value Proposition Guide: Describes key features of patient-centered design innovation.

2. **Early and frequent engagement from all key stakeholders – including sponsors, patients, regulators, and many others – is critical for successful collaboration, problem solving, and planning.**

A master protocol approach requires the coordination of many internal cross-functional units and external stakeholders – the success of a master protocol study hinges on regular communications and collaboration between all these different groups during design and execution phases. Sponsors of master protocol studies should spend significant time engaging with all stakeholders about the unique design and operational features of their master protocol studies.

Related CTTI Tools

- **Master Protocol Content Development Guide:** Provides a list of key stakeholders that should be engaged in the development of the written protocols and sub-protocols.
- **Simulation Tool:** Describes how statistical simulation can be used as a tool for communication and decision making across multiple stakeholders.
- **FDA Engagement Tool:** Describes key mechanisms that can facilitate early and frequent interaction with the FDA during the pre-planning and planning stages of study development
- **Master Protocol References & Resources:** A list of articles, webinars, and other resources that provide a basic overview of adaptive platform, umbrella, and basket master protocol designs.
- **Study Execution Case Studies:** Provides an overview of how study teams work collaboratively with internal and external stakeholders to address major challenges during the study execution phase.

3. **Develop centralized and standardized operational processes that facilitate the successful implementation of adaptive study designs.**

Organizations leading the development of master protocol studies need to conduct an important balancing act: maintaining a flexible and agile study design within a highly coordinated and centralized operational infrastructure. This tension between iterative, cyclical innovation and the need for centralization will impact core operational aspects of a master protocol study across its lifecycle. As such, operational teams and design teams need to work close together to ensure that the innovative design can be implemented.

Related CTTI Tools:

- **High-Level Roadmap:** provides a list of key operational action items in the pre-planning and planning phase.
- **Master Protocol Development Guide:** Describes key operational processes that are triggered as the written protocol and sub-protocols are drafted.
- **Operational Partner Assessment Tool:** Provides a list of key factors that should be used to assess operational partners' ability to fulfill key operational functions in the trial.

4. Share lessons learned to drive adoption.

All master protocol studies are different and will face a unique challenge. As uptake of master protocol studies occurs, there will be an ongoing need for study teams to share their lessons learned and related resources publicly, in an effort to advance the master protocol concept in diverse disease areas and across regulatory agencies.

Sponsors such as patient advocacy groups and academic institutions have an especially critical role to demonstrate strategies that yield unprecedented collaboration across stakeholders in the clinical trial ecosystem to address the unmet patient needs. Lessons learned and resources related to stakeholder engagement and strategic partnership consolidation are needed to build future early adopters' capacity to leverage master protocol studies in diverse disease areas.