



DIGITAL HEALTH TRIALS

Recommendations to Sponsors for Planning Decentralized Trials

CTTI defines decentralized clinical trials (DCTs) as those in which some or all study assessments or visits are conducted at locations other than the investigator site via any or all of the following **DCT elements**: tele-visits; mobile or local healthcare providers, including local labs and imaging centers; and home delivery of investigational products.

Decentralized clinical trials can be completely remote or partially decentralized with hybrid approaches. Hybrid trials are those that require some visits to be conducted on site, while other visits or assessments can be performed at a participant's home or within their local care community. Fully remote trials have no required site visits.

DCT elements are often used together with digital health technologies, which are discussed separately at [CTTI's Digital Health Trials \(DHT\) Hub](#).

RECOMMENDATIONS

1. Engage All Stakeholders, Early & Often

Collaboratively consider the needs of [all stakeholders](#)—including internal stakeholders (e.g., biostatisticians, pharmacovigilance) and external stakeholders, such as patients, clinical investigators and other site staff, IRBs/IECs, operational partners, and regulators—iteratively from the earliest stages of study design.

Considerations for trials incorporating DCT elements include:

- ▶ Engage patients and site personnel to assess their needs and expectations related to each DCT element, including the appropriateness and acceptability for the planned participant population; any options for completing planned assessments (e.g., going to site vs. local clinic); and all aspects of trial design and execution.
- ▶ Build in time for early consultation with regulators/health authorities to discuss novel elements considered critical to quality.
- ▶ Involve in-country experts to evaluate variabilities in the laws, regulations, and operational feasibility within each planned study country related to planned DCT elements. Be aware that there may be variation within each country as well (e.g., state-by-state variation in telehealth licensing requirements within the US).

- ▶ Engage technology providers early in study design to ensure an understanding of operational challenges and to confirm capabilities to manage these. Begin contracting and any vendor qualification processes at the earliest possible opportunity.
- ▶ For studies that include DCT elements new to the sponsor or CRO, conduct a protocol simulation (i.e., a “dry run”) with key stakeholders (including patients and site personnel) in order to detect potential issues with DCT elements and associated platforms/technologies.

2. Plan Ahead

All trials should follow a [Quality by Design](#) approach that translates insights from trial stakeholders into an optimized trial design and reduces opportunities for errors that have a meaningful impact on the safety of trial participants or the credibility of the results. Considerations for designing trials that incorporate DCT elements include:

- ▶ At the earliest stages of study design, ideally as part of the clinical development plan, assess which potential study activities are feasible and suitable to conduct remotely. The suitability of the investigational product for home delivery and/or administration will be a significant determinant for how decentralized the trial can be.
- ▶ As the study design evolves, identify and plan to incorporate those DCT elements that are likely to provide an overall benefit to the study or the participants’ trial experience (e.g., offering options for completing assessments at home, which may also increase retention) while maintaining safety oversight and ensuring data quality. Holistically assess the benefits vs. the challenges and costs.
- ▶ Incorporate flexibility, where feasible, at all levels of the trial (e.g., study participant options for remote vs. in-person visits; site-by-site options for use of DCT elements or telehealth platforms; country-by-country variation to reflect local laws and regulations), while balancing any added operational complexity and/or risk to data quality.
- ▶ Plan study budgets holistically, recognizing that costs are likely to be distributed differently than in traditional trials and that current budgeting approaches may not adequately account for these differences.
- ▶ Assess the experience and capabilities of each vendor, site, and local/mobile healthcare provider with the planned DCT elements; be prepared to provide appropriate initial and ongoing (or on-demand) training that is tailored to the

needs of each stakeholder.

3. Address Important Risks to Study Quality

As with all trials, monitoring and other oversight plans should be developed that focus on mitigating important risks not addressed through trial design and/or that may arise from trial implementation. Considerations for trials incorporating DCT elements include:

- ▶ When using multiple local facilities, community healthcare centers, and/or mobile nurses, ensure that oversight plans include mechanisms for monitoring the consistency and comparability of data collection and consult with relevant health authorities as early as possible.
- ▶ As with all trials, ensure third-party (e.g., vendor) oversight addresses quality and adherence to GCP, compliance, financial oversight, and well-qualified and sufficient resourcing.
- ▶ Understand where requiring the use of DCT elements may limit patient access, participation, and diversity and establish appropriate plans for patient outreach, education, and technical support.
- ▶ Evaluate and address risks to the study participants' privacy and confidentiality that may arise from the incorporation of DCT elements (e.g., risks related to home delivery and administration of investigational product).
- ▶ Clearly define responsibilities for triaging and evaluating data to ensure adequate protection of participant safety, as well as for adverse event reporting (according to the requirements in each planned study country).
- ▶ Ensure that all technologies and associated platforms involved in DCT elements have been thoroughly tested by the end users. Plan how to handle system failures at any level (e.g., from connectivity issues for individual study participants up through study-wide platform failures).
- ▶ Tailor the monitoring plan to address any study-specific human subject protection and data integrity risks related to incorporation of DCT elements (e.g., technical failures, declining protocol adherence, data quality issues) that require resolution before they compromise the study.

RESOURCES

- ▶ [Clearing a Path for Broad Implementation of DCTs](#)
- ▶ [Considerations for Delivering an Investigational Product](#)