MRCT CENTER
THE MULTI-REGIONAL CLINICAL TRIALS CENTER OF BRIGHAM AND WOMEN'S HOSPITAL AND HARVARD

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Proportionate Oversight in Decentralized Clinical Trials

How These Four Documents Work Together:

A Practical Guide for Sponsors, Investigators, and HCPs

The introduction of decentralized elements in clinical trials requires attention to both study design and its execution. These four documents form an integrated operational system. Each has a distinct function, and they are meant to be used in sequence, feeding into one another.

Optimizing DCTs

SPONSORS

Sponsors should start with the *Optimizing DCTs* document. Before a single participant is enrolled, the sponsor must determine which trial elements can be moved away from the clinical trial site and closer to the participant: the participant's home, a local clinic or imaging facility, and/or a community pharmacy. The *Optimizing DCTs* document walks through that process systematically. It asks the sponsor to identify critical-to-quality (CTQ) factors—the data points and procedures where errors actually matter, where a misstep could compromise participant safety or render an endpoint uninterpretable. For each candidate decentralized clinical trial (DCT) element, the sponsor must assess feasibility and reliability: Can eligibility be confirmed remotely? Can the investigational product (IP) be safely shipped and self-administered? Can the primary endpoint be reliably captured outside the clinic? If the answer is yes, the element belongs in a decentralized workflow—with proportionate controls in place. This document is the sponsor's tool for decentralized elements. It should be worked through during protocol development, not retrofitted afterward.

Proportionate Oversight Framework

INVESTIGATORS

***The Framework* document is where sponsor decisions become investigator action.** Once CTQ factors are defined and communicated, the investigator picks up the baton. *The Proportionate Oversight Framework* translates the sponsor's CTQ factors and risks relevant to the investigator's tasks, duties, and functions in the trial into a calibrated, site-level oversight plan. It organizes the investigator's thinking across four interrelated domains: participant characteristics (who they are, where they live, how complex their condition), the nature of the trial (phase, design, endpoint structure), the research site's own staff and infrastructure, and the IP itself (how well understood, how administered, how stored). The investigator weighs these domains together—not one at a time—because risk compounds across them. A vulnerable participant population, combined with a novel IP and inexperienced site staff, presents a fundamentally different risk profile than any one of those factors in isolation. The *Framework* produces an integrated oversight plan: who talks to whom, how often, through what channels, and with what escalation pathways when something goes wrong. It is a living document; it should be revisited as trial data accumulates and the operational picture evolves.

HCP Instruction Sheet

SPONSORS

INVESTIGATORS

HCP

* The sponsor should complete the trial-specific information, and the investigator should complete the participant information, both to be provided to the HCP

When a healthcare provider (HCP) enters the picture, the *HCP Instruction Sheet* is their operating document. Local HCPs—primary care providers, community cardiologists, home health nurses—are often the people actually in the room with trial participants between site visits. If local HCPs perform activities that require detailed knowledge of the protocol, the investigator's brochure, or other trial-related documents, they should be formally listed on the delegation log as part of the study team and appropriately trained. These distinctions are described in ICH E6(R3). Alternatively, if they don't require a detailed knowledge of the protocol but what they need is clear, actionable, pre-filled instructions (e.g., the participant identity, what procedures to perform, how to document and transmit findings, and whom to call when something unexpected happens), then the *HCP Instruction Sheet* is that document. It is designed tço be completed collaboratively by the sponsor and the research site before it reaches the HCP's hands—green and orange colored text place holders mark every field requiring site or sponsor input prior to delivery to the HCP. The HCP reads it, performs the visit, documents the findings, and transmits them to the research site. Their role is precise and bounded. That boundary protects both the participant and the integrity of the research.

HCP Check-in Questions for Participants

HCP

The *HCP Participant Check-In Questions* are the HCP's structured guide for routine participant visits.

However well-designed a trial is, the unexpected may occur.

During a decentralized clinical trial, important safety, adherence, and study-related concerns may emerge through conversations with participants. A participant may report a change in health, a new medication, difficulty taking or storing study medication, a missed procedure, possible pregnancy, or another issue that may require follow-up.

The document helps the HCP consistently ask key questions, record the participant's response, and identify the appropriate immediate action. Across each check-in topic, the essential message remains the same: the HCP provides any necessary and appropriate clinical care, documents what was reported or observed, and promptly contacts the research site when a clinical or study-related concern arises. The HCP does not make protocol decisions—such as decisions about study medication continuation, eligibility, or causality. Those determinations remain with the investigator and sponsor.

Keeping the document brief, structured, and easy to scan is deliberate. An HCP conducting a participant visit needs a practical tool that supports a consistent conversation and provides clear direction: what should I ask, what should I document, and when should I contact the research site?

Together, these four documents represent a coherent, integrated system for decentralized trial conduct—sponsor-driven design, investigator-calibrated oversight, HCP-executed delivery, and a clear escalation structure when reality diverges from plan.

You can view all of the Tools on the MRCT Center website:

https://mrctcenter.org/resource/proportionate-oversight-in-decentralized-clinical-trials-dcts/