

# Designing the Operating Model Around the Therapy

## *A Practical Framework for Complex Clinical Trials*

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### **Executive Perspective**

A clinical development plan establishes what a program needs to learn. Its operating model determines how patients, investigators, sites, and service providers will make that learning possible. Sponsors should design those arrangements while the protocol, delivery partners, and budget can still be shaped together.

A scientifically sound protocol can place demands on families that are difficult to sustain. An experienced center may lack the staffing, scheduling capacity, or referral pathway required for a particular study. Several capable vendors may each deliver their contracted service while leaving the decisions between organizations unresolved.

For rare diseases, oncology, advanced therapies, and other operationally complex programs, Tanner Clinical Consulting recommends an approach that examines each activity: establish what each important study activity requires, where it should occur, who is accountable, and how it connects with the participant's wider care and study experience.

The approach described here is a practical planning framework for sponsors and their partners. It combines patient and caregiver input, site feasibility, clinical requirements, and commercial considerations. It is intended to expose assumptions early and guide implementation; it is not a validated model for predicting enrollment, retention, or financial outcomes.

The result should be an operating model brief that answers five questions: What must the study deliver? What does participation require? Which capabilities are genuinely available? How will decisions and information move between organizations? What resources and contingencies are needed to sustain the model?

### **1. Translate Scientific Intent Into Delivery Requirements**

Broad labels such as traditional, hybrid, and decentralized do not resolve the decisions that make a protocol executable. A program requiring a specialist procedure, tightly scheduled assessments, and extended follow-up still needs a clear rationale for where each activity belongs.

Begin with the factors essential to participant protection and interpretable results. Identify the assessments, decisions, and timing requirements that deserve the greatest operational attention. ICH E6(R3) emphasizes quality by design and approaches proportionate to risk and the importance of the data, while avoiding unnecessary burden on participants and investigators.<sup>[1]</sup>

For each critical activity, document the required expertise, equipment, location, timing, responsible role, result review, and contingency. Review these decisions jointly with clinical development, operations, medical, statistics, data management, regulatory, and relevant site personnel. This helps distinguish what the protocol requires from what a familiar delivery model happens to provide.

The brief should also identify dependencies and uncertainties. If the enrollment forecast assumes that a procedure room, specialist, and product will be available within the same narrow window, that assumption requires confirmation. Assign an owner and a decision date to unresolved items, and show their implications for cost, timing, and participant experience.

## 2. Design Participation Around The Patient And Family

A schedule of assessments describes what the study asks participants to do. It does not fully describe what participation asks of their lives. A brief appointment may require a day away from work, transport arrangements, overnight accommodation, and care for other family members.

Map the journey from referral and screening through treatment and follow-up. Consider clinical burden, including procedures and recovery; practical burden, including travel and expense; and coordination burden, including appointments, paperwork, and communication across organizations.

For pediatric programs, this assessment should include the family unit. School schedules, siblings, caregiver employment, the child's tolerance of prolonged visits, and communication appropriate to the child's age all deserve consideration. An available appointment is not necessarily a manageable appointment.

Review whether assessments can be consolidated, unnecessary duplication removed, or study visits aligned with routine care, where scientifically and operationally appropriate. Longer combined visits also have costs: fewer journeys may mean more fatigue or a less reliable assessment. Test the complete experience with patients, caregivers, and site teams rather than assuming that fewer visits always means less burden.

Support must be usable when it is needed. Reimbursement may eventually cover an expense while still requiring a family to pay upfront. Travel services may require more notice than the study's scheduling process allows. TCC recommends clear booking and payment arrangements, an understandable escalation route, and a consistent contact who can coordinate practical questions without displacing the clinical team's responsibilities.

Participation must remain voluntary. The aim is to remove avoidable barriers and support informed choices, not to promise therapeutic benefit or pressure families to remain in a study.

## 3. Select Sites For The Complete Delivery Pathway

A center's reputation and therapeutic experience are useful starting points. Selection also requires evidence that it can perform the work of this protocol with its current resources and competing commitments.

Patient access needs similar scrutiny. A reported patient population is the beginning of an enrollment assessment. Sponsors still need to examine eligibility, referral pathways, competing research, willingness to participate, and the practical ability to attend required visits. These assumptions should remain visible in the forecast.

| Capability        | Evidence to seek during feasibility                                                                  |
|-------------------|------------------------------------------------------------------------------------------------------|
| Patient access    | A credible identification and referral pathway, with assumptions about eligibility and participation |
| Clinical delivery | Named specialists, facilities, supporting services, and scheduling arrangements                      |
| Research capacity | Coordinator coverage, workload, competing studies, and backup arrangements                           |

| Capability               | Evidence to seek during feasibility                                                      |
|--------------------------|------------------------------------------------------------------------------------------|
| Assessment quality       | Appropriate equipment, trained personnel, and consistent methods within protocol windows |
| Product handling         | Applicable storage, preparation, accountability, and administration capabilities         |
| Continuing participation | Follow-up ownership, local care coordination, and support for distant participants       |

Site workload and patient experience should be assessed together. A new outside service may reduce visits but leave coordinators arranging appointments, resolving queries, and reconciling records. Feasibility should estimate that work and identify the resources needed to absorb it.

Country selection should test whether the proposed services and referral arrangements are locally workable. A common clinical standard may require different implementation arrangements across countries. Those differences belong in the operating plan and budget, with local regulatory, professional, and institutional requirements assessed before activation.

## 4. Map Treatment Dependencies And Rehearse Exceptions

For programs with tightly linked treatment activities, develop a dependency map connecting eligibility confirmation, product availability, participant preparation, specialist staffing, treatment scheduling, and observation. Identify which changes require a clinical decision and which require logistical coordination.

Some cell and gene therapy programs add manufacturing, transport, identity, custody, or handling considerations specific to the product. The exact controls must follow the product and protocol; a process designed for one therapy should not be assumed suitable for another.

A postponement is a useful readiness test. Who determines whether screening assessments need repeating? Who confirms that the product and clinical team remain ready? Who tells the family, rearranges transport, and authorizes additional costs? What information must reach each party before a new treatment date is confirmed?

Resolve these questions before the first participant encounters them. A readiness exercise should test the full sequence, including the handoffs between departments. Individual services can be ready while their combined workflow remains untested.

## 5. Allocate Activities According To Safety And Evidence Needs

Evaluate each proposed location against participant safety, assessment reliability, available capability, information flow, and the total experience of participation. An outside service should have a clear purpose and a workable connection to the responsible investigator.

FDA guidance recognizes that administration or complex assessments may need to occur at a traditional site while suitable activities occur remotely or locally. Applicable regulatory requirements remain the same for trials with decentralized elements. The guidance addresses the associated planning, sponsor and investigator responsibilities, and safety oversight.<sup>[2]</sup>

Clinical and statistical review should precede a change in assessment method or setting. Equipment, raters, sample processing, and conditions of measurement may affect how a result can be interpreted. An assessment that can be performed at home is not automatically interchangeable with one performed at the site.

For digital measures, selection should begin with the intended use and population. FDA's digital health technology guidance addresses verification, validation, usability, and other considerations for remote data acquisition.<sup>[3]</sup> Technology also needs an operational plan for training, connectivity problems, replacement devices, missing data, and participants who cannot use the proposed method.

Specify a fallback before introducing the activity. If a local provider becomes unavailable or an assessment cannot be completed remotely, the team should know how to respond while preserving appropriate care and the study's evidence requirements.

## **6. Assign Ownership Across Organizational Boundaries**

The operating model should show how information becomes a decision. An uploaded laboratory result is not evidence that the appropriate clinician has reviewed it. A completed home visit is not proof that a concern has reached the investigator.

For critical workflows, define who initiates the activity, confirms completion, reviews the output, and acts on it. Identify the authoritative record, expected review timing, escalation route, and backup coverage. Urgent clinical information needs an appropriate response pathway, including outside routine hours; routine information needs a defined review process.

These arrangements should be consistent across the protocol's implementation documents, vendor scopes, agreements, training, and site procedures. A responsibility matrix is useful only when the people doing the work understand it and can carry it out.

Coordination should also be visible to participants. Families should know whom to contact for clinical concerns and practical support, and how the study relates to their usual care. Avoid requiring them to resolve disagreements between providers or decide which organization owns a missed activity.

## **7. Plan Continuity And Future Evidence Needs Early**

For studies with extended follow-up, continuity needs an owner, resources, and a durable process. Families may move, caregivers may change, children may transition into adult care, and investigators may leave an institution. Planning should cover updated contact details, authorized record access, team transfers, and communication preferences.

For gene therapy, FDA recommends a risk assessment specific to the product to inform observation over the longer term for delayed adverse events. Duration and procedures should follow the relevant product and program considerations rather than a universal assumption applied to all therapies.<sup>[4]</sup>

Distinguish follow-up needed to evaluate efficacy or durability from surveillance intended to identify delayed risks. The activities may overlap, but their evidence objectives, expertise, and budgets may differ. Suitable local or remote contacts can be considered where they meet those objectives and maintain appropriate oversight.

The same planning discipline should extend to later development. TCC recommends early discussion across functions of the evidence and delivery questions that may matter beyond the current trial: relevance of outcomes, capacity in the intended treatment settings, continuing data needs, and the likely participation pathway at larger scale. Medical affairs, market access, and patient representatives can help identify questions without turning the trial into a collection of unrelated objectives.

Additional assessments or data sources should have a defined purpose. Registries, observational research, expanded access, and confirmatory trials are distinct activities; one should not be treated as an automatic

substitute for another. Their suitability and any future commitments require evaluation for the individual program.

## 8. Make Commercial Assumptions Explicit

Vendor proposals are easier to compare when sponsors have established a common set of delivery assumptions. One bidder may include participant travel coordination while another assumes the sites provide it. One may price local assessments while another budgets for every activity at the investigative center.

Define the required service, its interfaces, and its expected volume before comparing prices. Include sponsor coordination, site administration, data reconciliation, participant support, and contingencies. Ask vendors to challenge unrealistic assumptions with evidence and explain the consequences of their proposed alternatives.

Test the budget against a few plausible scenarios: slower enrollment, a treatment postponement, repeat assessments, additional travel support, or replacement of an outside provider. A low unit price does not capture the full cost of an arrangement that creates repeated work elsewhere.

Planning for scale also means testing what changes when more sites or countries join. A process dependent on informal calls among a small expert team may need a clearer governance structure, training plan, and capacity model before expansion. The objective is a budget and delivery plan built on the same assumptions.

## 9. Apply The Framework To A Participant Pathway

The following example is illustrative. It does not describe a specific study or demonstrate an outcome.

Consider an early phase program for a rare disease requiring specialist administration, frequent initial assessments, and extended follow-up. Potential participants live several hours from the treating center. The sponsor must preserve the necessary clinical and assessment controls while making the pathway manageable for those families.

| Stage                  | Decision to resolve                                    | Practical output                                                                              |
|------------------------|--------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| Referral and screening | What information can be reviewed before travel?        | Preliminary records review that does not replace required consent or eligibility confirmation |
| Treatment preparation  | Which services must be ready together?                 | Readiness check with ownership of postponement decisions                                      |
| Initial follow-up      | Which assessments require the center?                  | Visit plan linked to clinical risk and measurement requirements                               |
| Later participation    | Which activities can be completed locally or remotely? | Instructions for each activity, suitable providers, and defined result review                 |
| Extended follow-up     | How will contact and responsibility remain continuous? | Named ownership, contact maintenance, and transfer arrangements                               |

The exercise should produce decisions for site qualification, service scopes, participant materials, and the budget. Proposed capabilities remain assumptions until verified. Where uncertainty persists, the brief should identify the consequence, owner, and next decision rather than present a provisional arrangement as established fact.

## 10. Review Performance And Act On The Causes

An operating model begins with informed decisions and assumptions. Study conduct tests them. Select a small number of measures linked to the model's purpose, with clear definitions and proportionate collection effort.

| Intended function         | Possible measure                                                      |
|---------------------------|-----------------------------------------------------------------------|
| Manageable participation  | Travel days, coordination difficulties, and reasons for missed visits |
| Timely assessments        | Assessments outside protocol windows and their causes                 |
| Reliable handoffs         | Delayed reviews, incomplete transfers, and unresolved ownership       |
| Sustainable site capacity | Scheduling constraints, workload concerns, and recurring service gaps |
| Continuing participation  | Withdrawal reasons and barriers to using support                      |
| Financial visibility      | Repeat activities, unplanned travel, and changes in contracted scope  |

These are proposed management measures, not validated predictors of study success. Interpret them with context. A missed visit may reflect illness, transport failure, scheduling difficulty, or a decision to discontinue. Those causes require different responses, and withdrawal should not automatically be attributed to operational failure.

Review should lead to decisions. If remote activities repeatedly require corrective site visits, examine the assessment process. If transport assistance is rarely used despite reported difficulties, examine access to that support. Define who reviews recurring problems and when a change must be considered, following applicable protocol, approval, oversight, and documentation processes.

### From A Clinical Plan To A Deliverable Study

Before committing to a delivery structure, sponsors should be able to explain where critical activities will occur, why those settings are appropriate, how participants will navigate the pathway, and who will act when the plan encounters a problem.

The operating model brief brings those decisions together. It should guide site selection, vendor evaluation, realistic budgeting, and team preparation, then remain a reference as the program evolves.

Tanner Clinical Consulting's approach connects scientific intent with the people, capabilities, and processes required to deliver it. A clinical plan becomes executable when its assumptions have been translated into clear responsibilities, workable processes, and a participation pathway that patients and sites can realistically manage.

## References

1. International Council for Harmonisation. E6(R3) Guideline for Good Clinical Practice. Principles and Annex 1. Adopted January 6, 2025; corrected October 24, 2025. Principles 6 and 7 address quality by design and proportionality.

[Read the guidance](#)

2. U.S. Food and Drug Administration. Conducting Clinical Trials With Decentralized Elements. Guidance for Industry, Investigators, and Other Interested Parties. September 2024. Sections III.A, III.B, III.D, and III.I.

[Read the guidance](#)

3. U.S. Food and Drug Administration. Digital Health Technologies for Remote Data Acquisition in Clinical Investigations. Guidance for Industry, Investigators, and Other Stakeholders. December 2023.

[Read the guidance](#)

4. U.S. Food and Drug Administration. Long Term Follow-Up After Administration of Human Gene Therapy Products. Guidance for Industry. January 2020.

[Read the guidance](#)

Regulatory sources accessed September 30, 2026. The operational framework and illustrative example are the author's recommendations. Application should reflect the protocol, product, population, and requirements of each participating jurisdiction.