# Enhancing Participation in Clinical Trials

How sponsors can operationalize the FDA's guidance with ClinSphere® Trial IntelX™

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# Contents

# Designing More Inclusive Clinical Trials

Recent FDA guidance emphasizes the need for clinical trials that reflect real-world patient populations. The challenge for sponsors is how to design protocols that balance representativeness across demographic and clinical characteristics with operational feasibility.

This ebook considers the impact of the new guidance and explores how ClinSphere® Trial IntelX™ provides the cross-industry intelligence sponsors need to design modern, inclusive trials that work from the start.

# Summary of the FDA Guidance

In December 2025, the U.S. Food and Drug Administration (CDER/CBER) finalized its **Enhancing Participation in Clinical Trials — Eligibility Criteria, Enrollment Practices, and Trial Designs** guidance (Docket FDA2019D1264). The goal is clear: help sponsors design and conduct trials that reflect real-world patient populations through inclusive eligibility, practical enrollment and retention practices, and modern, flexible trial designs.

The guidance reframes "diversity" as representativeness, explicitly encompassing both demographic characteristics (sex, race, ethnicity, age and geography) and non-demographic factors (organ dysfunction, comorbidities, disabilities, extremes of body weight and low-prevalence conditions). It underscores that enrolling participants across a wide range of baseline characteristics improves generalizability, allows detection of subgroup signals and informs how therapies are used after approval.

Practically, it calls on sponsors to:

- **Broaden eligibility criteria** by removing unjustified exclusions and reevaluating criteria as safety knowledge accumulates
- **Reduce burden and increase accessibility** by minimizing unnecessary visits, offering flexible scheduling and decentralized elements, and providing multilingual materials and reimbursement for reasonable expenses
- **Adopt designs that support inclusion,** including prespecified adaptations and early pharmacokinetics/pharmacodynamics (PK/PD) characterization to safely include medically complex patients
- **Plan for subgroup insights** that inform labeling and real-world use

This guidance arrives alongside the modernization of global good clinical practice principles in ICH E6(R3), which emphasizes flexibility, proportionality and risk-based quality management — further enabling inclusive designs and innovative trial operations.

# Challenges the Industry Faces with Clinical Trial Participation Today

There is widespread commitment to equitable research among sponsors and CROs to overcome systemic barriers that can hinder participation and representativeness. These challenges include:

## 01

### Legacy Eligibility and Procedural Complexity

Many protocols carry forward conservative exclusions, such as age ceilings, rigid comorbidity cutoffs or burdensome assessment schedules, that originated in earlier phases or past programs. Overly restrictive criteria can shrink the eligible pool, skew representation and create downstream operational risk (screen failures, deviations, slow recruitment and amendments). Sponsors often lack comparative evidence to justify relaxing criteria without compromising safety or interpretability.

## 02

### Participant and Site Burden Is Hard to Quantify in Advance

Sponsors and CROs recognize that frequent visits, lengthy assessments and complex documentation deter participation. Yet quantifying "burden" and simulating alternative designs at planning time remains difficult without cross-trial benchmarks and analytics that link protocol elements to actual outcomes (enrollment velocity, duration, deviations and dropout). Without those lenses, burden reduction becomes reactive, addressed only after signals emerge during conduct.

## 03

### Placement Decisions Under Uncertainty

Choosing countries, sites and investigators who can enroll representative participants and execute inclusive practices is challenging at start-up. Identifying where eligible patients exist is just part of the equation. Historical performance can help reveal whether sites and PIs can actually recruit them. Sponsors need multifactor evidence — historical performance, protocol fit, capacity and competitive context — to place trials where participation can thrive.

## 04

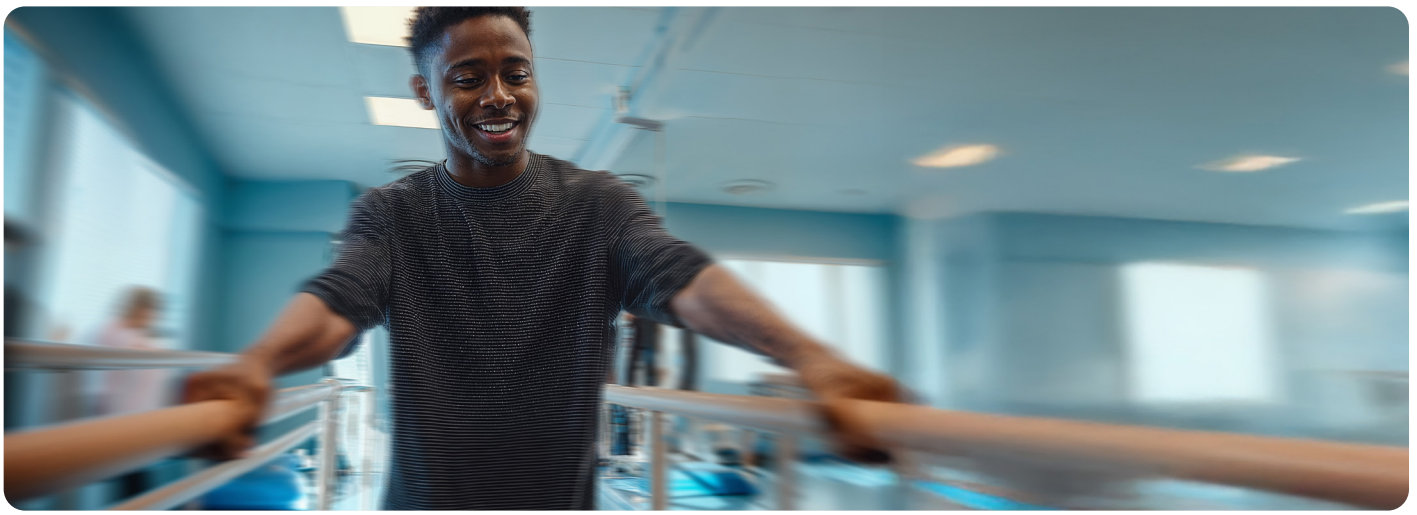
### Limited Foresight Into Subgroup Signals and Timelines

Traditional forecasting methods rarely integrate protocol features, historical outcomes and site performance at scale. As a result, teams lack predictive visibility into enrollment bottlenecks, duration drivers and the conditions under which subgroup signal detection is plausible, limiting the ability to set inclusive targets and manage them proactively.

## 05

### Process and Culture Change

Inclusive participation is not just a design problem; it's an operational and cultural commitment across sponsors, CROs and sites. Teams need consistent, data-driven decision support and input from all stakeholders that translates guidance principles into day one choices — eligibility language, visit schedules, compensation, and country and site selection decisions — so inclusion is a built-in quality attribute, not an add-on.



# How ClinSphere® Trial IntelX™ Addresses These Challenges Before They Arise

WCG's ClinSphere® Trial IntelX™ is an AI-powered trial intelligence platform that transforms cross-trial data into prestart design guidance. It equips sponsors and CROs to align with the FDA's participation guidance from the first protocol draft.

Trial IntelX™ draws on WCG's unparalleled data assets, including 80,000+ complete protocols, 40,000+ benchmarked trials, and deep operational insights from global site relationships and patient advocacy efforts to forecast outcomes and recommend design, country and site selection decisions that reduce burden and improve representativeness.

The capabilities of Trial IntelX™ map directly to the guidance's key recommendations:

### 1) Broaden Eligibility with Evidence, Not Guesswork

**What the guidance asks:** Reevaluate exclusion criteria and enroll participants who mirror real-world users.

**How Trial IntelX™ helps: Protocol burden and complexity scoring** surfaces where inclusion is artificially constrained — highlighting criteria, procedures and documentation elements that may create avoidable barriers. Comparative analytics show how protocols stack up against peer trials in similar indications, revealing protocol design outliers, highlighting where simplification would expand eligibility, and reducing participant and site burden without diluting scientific integrity. That translates to actionable redlines before a protocol reaches finalization.

### 2) Reduce Participant and Site Burden Quantitatively

**What the guidance asks:** Make participation less burdensome; use flexible scheduling and decentralized elements; provide accessible materials and reimburse reasonable expenses.

**How Trial IntelX™ helps:** Trial IntelX™ turns burden into a **measurable design attribute.** Its dashboards quantify visit frequency, assessment duration and logistics to model the participant experience. Teams can simulate alternative schedules (e.g., consolidating visits, remote assessments or streamlined labs), see the downstream impact on enrollment and dropout, and choose the least burdensome path that still meets scientific endpoints. This prevents later amendments and helps sponsors plan operational supports (language, travel, scheduling windows) at start-up.

## 3) Place Trials Where Representativeness and Performance Intersect

**What the guidance asks:** Expand access geographically; plan where trials run to reduce burden and increase inclusiveness.

**How Trial IntelX™ helps:** The **Country and Site Optimizer** ranks geographies, sites and Principal Investigators (PIs) using historical performance, protocol scoring, competitive intelligence, historical demographic enrollment and experience profiles. Instead of relying solely on prior relationships or single dimension feasibility, sponsors can select high-fit locations where eligible patients and capable operations meet, accelerating enrollment and improving representativeness. This evidence-based placement helps mitigate screen failures and start-up delays while fostering community-level accessibility aligned to the guidance.

## 4) Plan for Subgroup Insights and Realistic Timelines Up-Front

**What the guidance asks:** Design for meaningful subgroup analysis across demographic and clinical strata; ensure trials reflect real-world users.

**How Trial IntelX™ helps:** Trial IntelX™'s portfolio-level views and forecasting models show **predictive drivers** of trial duration and enrollment across indications, demographics and site archetypes. Teams can set inclusive enrollment targets, evaluate whether subgroup detection is feasible within planned timelines, and adjust design or placement before first patient in. By connecting protocol decisions with likely outcomes, sponsors create transparent, defensible plans for representativeness and signal detection that align with FDA expectations.

# Why Alignment Matters, and Why It's Now Possible

The FDA's guidance asks sponsors to do more than publish commitments – it asks them to operationalize inclusion at every planning step. That used to require broad assumptions or retrospective fixes. With Trial IntelX™, it becomes data-driven and proactive:

**From Intention to Evidence**

Trial IntelX™ quantifies burden, compares eligibility and forecasts operational performance outcomes using one of the industry's richest protocol and performance datasets, turning inclusive design from principle into practice.

**From Reactive Fixes to Prespecified Adaptability**

By correlating protocol elements to real-world outcomes, Trial IntelX™ helps teams design adaptive pathways that enable broader participation.

**From Generic Feasibility to Strategic Placement**

Country/site ranking is grounded in multidimensional fit (experience, historical capacity and protocol demands), so access and performance aren't trade-offs; they're mutually reinforcing.

CONCLUSION

# Designing For Inclusion From the Start

Inclusive, representative trials are not only ethically imperative; they're essential for credible evidence and real-world relevance. The FDA's 2025 guidance provides the "what" and "why." ClinSphere® Trial IntelX™ delivers the "how" — a way to design for inclusion before issues arise.

By quantifying burden, comparing eligibility, forecasting timelines and enrollment, and placing trials where eligible patients, qualified investigators and capable sites intersect, Trial IntelX™ gives sponsors and CROs the decision support they need to align with FDA expectations from day one.

Experience the difference Trial IntelX™ can make for your protocol design at wcgclinical.com/knowing and schedule a demo.