

Multiregional Oncology Trials: Top Takeaways from a Former Regulator

Harpreet Singh, MD, Precision for Medicine Chief Medical Officer and former FDA Division Director for Oncology, authored a comprehensive whitepaper on Multiregional Clinical Trials (MRCTs). This resource contains data and insights to help biopharma companies optimize the design of their trial strategy to meet FDA expectations.

1

Representativeness Matters More Than Geography

Insight: FDA evaluates whether trial populations reflect U.S. patients—not just whether the trial is multiregional.

Action: Design trials with demographic, genetic, and clinical characteristics aligned to U.S. standards of care. Include sufficient U.S. enrollment or justify generalizability with strong scientific rationale.

2

Consistency Across Regional Subgroups Is Critical

Insight: Geographic diversity alone does not guarantee success; inconsistent efficacy signals across regions can derail approval (e.g., STARGLO case).

Action: Power MRCTs for subgroup analyses and monitor interim data for regional heterogeneity. Be prepared to explain differences scientifically.

3

Endpoint Selection Must Align with U.S. Regulatory Expectations

Insight: FDA prefers endpoints like overall survival (OS) over progression-free survival (PFS) when precedent exists (e.g., ORIENT-11 rejection).

Action: Align primary endpoints with U.S. standards early in protocol development. Discuss endpoint strategy with FDA during pre-IND or End-of-Phase 2 meetings.

4

Unmet Medical Need Can Drive Regulatory Flexibility

Insight: Single-country data may be acceptable in rare diseases or high unmet need scenarios (e.g., JUPITER-02 approval for NPC).

Action: Document unmet need rigorously and propose post-marketing commitments to address residual uncertainties in U.S. populations.

5

Early and Continuous FDA Engagement Is Non-Negotiable

Insight: Sponsors who engage FDA early on global strategy avoid costly redesigns and CRLs.

Action: Schedule early scientific advice meetings to confirm acceptability of foreign data, MRCT design, and subgroup plans.

6

Scientific Justification Is the Cornerstone

Insight: FDA expects robust evidence that foreign or multiregional data are biologically and clinically applicable to U.S. patients.

Action: Prepare detailed justification covering pharmacokinetics, disease biology, and treatment standards. Use exposure-response analyses and bridging data where needed.



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