

Master Protocols & IRT

5 Questions Sponsors Must Ask Before Selecting a Randomisation Partner

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Introduction

Master Protocols-including platform, umbrella, and basket trials-offer significant benefits and efficiencies in drug development compared with traditional trial protocols. However, their perpetual nature, adaptive designs, and evolving requirements make randomisation inherently more complex.

As a result, implementing and maintaining robust randomisation for Master Protocols can be challenging for sponsors. Selecting the right IRT provider is therefore critical.

This paper outlines five essential questions sponsors should ask when evaluating IRT providers for Master Protocols, with a focus on long-term trial success, regulatory readiness, and operational resilience.



1 Does the IRT provider have proven Master Protocol expertise?

A Master Protocol-naïve vendor is unlikely to effectively address the challenges of randomisation implementation and maintenance. An experienced provider will ask the right questions during the design phase, ensure flexible requirements are met, and have the tools and processes in place to support evolving randomisation needs throughout the life of the trial.

Almac has supported Master Protocols since their earliest adoption-well before formal regulatory guidance was established. With over a decade of experience, we bring deep expertise in designing, implementing, and maintaining randomisation strategies for adaptive, long running trials.

This experience is underpinned by two critical expert teams:

In-House Biostatistics Expertise

Almac's dedicated Biostatistics team focuses exclusively on randomisation and its implementation within IRT. This enables support for even the most sophisticated designs-including flexible randomisation, response adaptive randomisation, and minimisation-while ensuring seamless operational execution.

Adaptive Trial Design Center of Excellence (COE)

Almac's cross functional Centre of Excellence guides your Master Protocol through every stage of the trial. The COE provides comprehensive processes and tools to work closely with your team, ensuring smooth execution and ongoing support.

Key components include:

- ✓ **Protocol Review** – Our biostatisticians, drawing on experience from reviewing hundreds of protocols annually, ensure statistical randomisation requirements and adaptive features are appropriately integrated.
- ✓ **Risk Based IRT Design and Specification Reviews** – Our design team collaborates with yours to define the optimal implementation strategy, answer key design questions, and assess potential randomisation changes, including flexibility built into the initial IRT design where feasible.
- ✓ **Robust User Guides for Study Personnel** – As protocol adaptations introduce major differences compared with traditional trials, our guides enable site staff to administer the IRT effectively throughout the trial.
- ✓ **New Treatment Onboarding Checklists** – To manage the complex tasks associated with onboarding treatments and drug supply, structured checklists keep sponsors aligned with IRT and other systems, ensuring sites are ready for new treatments and supplies.
- ✓ **Ongoing Programme and Project Management** – Master Protocols operate in a continual amendment cycle. Our experienced project managers are trained to manage these complexities, keeping trials on track, on time, and within budget.

2 Does the IRT provider have the technology to support the complexity?

Master Protocols are transforming clinical development by improving efficiency, enabling adaptive learning, and streamlining operations. Still, these benefits also create randomisation challenges that basic IRT systems are not equipped to handle. These include:

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|  <p>Multiple Dimensions
(e.g., subpopulations, subprotocols, subgroups)</p> |  <p>Treatment Adaptations
(e.g., treatments added, paused, modified, re-entered, dropped)</p> |
|  <p>Treatment Allocation Ratios Adjustments
(e.g., due to shared control arms, higher performing treatments, treatments entering / exiting at different times)</p> |  <p>Varying Treatment Eligibility Criteria
(e.g., at different levels such as site, participant, biomarker, subgroup)</p> |

Without purpose built technology, sponsors risk fragmented methodologies, trial delays, and increased operational burden.

These randomisation challenges demand advanced system capabilities from the IRT provider. Almac's IRT technology offers a purpose-built solution to effectively meet the flexibility requirements of such randomisation:

- ✓ **Tailor-fit for your Master Protocol** – Almac can support any specific protocol requirement (e.g., multiple dimensions, treatment adaptations, ratio changes and eligibility).
- ✓ **Easy to Use** – Randomisation adaptations through a simple user interface.
- ✓ **Efficient** – Randomisation adaptations without trial disruptions or costly IRT amendments.
- ✓ **Easy to Understand** – Single, unified randomisation methodology for the life of the trial.
- ✓ **Inspection Ready Reports** – Clear transparency showing how randomisation adapted over time.
- ✓ **Trusted Methodology** – Implemented across dozens of Master Protocols in multiple therapeutic areas across a decade and refined based on experience and regulatory guidance.



3 How does the IRT provider manage frequent adaptations / amendments?

Since Master Protocols are designed to change overtime, it is critical for IRT providers to consider how to manage these changes. An inexperienced provider may build the IRT only based on initial randomisation (i.e., fixed schedule with set treatments and ratio), without flexibility. While this meets early needs, this creates burdens for Sponsors when the protocol adapts such as:



Generating new randomisation schedules



System downtime and trial delays



Fragmented randomisation methodologies across versions of the protocol



Costly / Lengthy IRT amendments



Substantial manual regulatory documentation

These burdens pose a barrier to the primary goal of Master Protocols – enhancing efficiency in drug development. Minimising trial disruptions and amendment costs are high priorities for Sponsors and should be addressed by the IRT provider.

Almac can implement a flexible randomisation process from the outset that can streamline adaptations, reducing both trial disruptions and amendment expenses. Since each protocol and Sponsor require varying degrees of flexibility based on their adaptation strategies, budgets, and timelines, the Almac team will work with your team during the planning phase to ensure alignment with your objectives – while maintaining open communication throughout the trial lifecycle.

4 How does the IRT provider address regulatory requirements?

Master Protocols are substantially more demanding from a regulatory perspective compared to traditional trials due to their adaptive designs and treatments entering and exiting the trial. The way randomisation is designed, documented, and managed in the IRT directly affects the complexity of regulatory reporting. For example, an inexperienced IRT provider might treat every randomisation change as an amendment, resulting in many system builds. This can make it difficult to explain multiple versions of randomisation functionalities and lists. In comparison, we make it easier to report randomisation through our flexible randomisation approach.

Almac's flexible randomisation approach aligns with regulatory guidance for Master Protocols by:

- ✓ Well-documenting randomisation process within specifications
- ✓ Using consistent methodology for the life of the trial
- ✓ Including robust reports that provide clear audit trail of randomisation assignments and how randomisation has evolved over the trial

Due to the stringent regulatory requirements surrounding randomisation integrity, especially with Master Protocols, consistent regulatory support from the IRT provider is essential throughout the trial lifecycle. Our knowledgeable Biostatistics team is well-equipped to deliver comprehensive regulatory assistance for randomisation, including providing guidance, monitoring, undergoing audits, facilitating reproducibility demonstrations, preparing TMF materials, and addressing other regulatory obligations.



5 Can the IRT provider support long lasting trials?

A Master Protocol may operate for years or even decades. Sponsors must carefully evaluate the stability of the IRT provider to ensure the company's continued presence throughout the trial's duration. Given that technology companies are subject to acquisitions and potential insolvency, it is essential for sponsors to choose IRT providers capable of demonstrating long-term viability and reliability.

Almac is a well-established IRT company with over 30 years of experience supporting complex clinical trials globally. As a privately owned organisation with a long-standing history, we provide sponsors with confidence that both expertise and technology will remain available for the duration of their programs - backed by continued investment in innovation and inspection ready delivery.

Conclusion

Master Protocols require more than a transactional IRT vendor - they require a long term randomisation partner. Selecting the right provider is critical to ensuring operational efficiency, regulatory readiness, and adaptability over the life of the trial.

By asking these questions, sponsors can evaluate whether an IRT provider is equipped to:

- ✓ Support adaptive design complexity
- ✓ Manage ongoing change efficiently
- ✓ Maintain regulatory confidence
- ✓ Deliver stability over long running programs

With proven Master Protocol experience, in house expertise, purpose built technology, and long term stability, Almac is the trusted IRT randomisation partner for Master Protocols.

About us

Almac is a global partner to the life sciences industry, providing services and technologies that support the development and delivery of medicines. We work closely with our customers to help bring therapies to patients worldwide.

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