EXECUTIVE SUMMARY

Improving Protocol Amendment Execution Through Site–Sponsor Alignment

Protocol amendments are a necessary mechanism to adapt clinical trials as science evolves. However, insights from a recent interactive session with research leaders across academic medical centers, health systems, and oncology programs highlight that the operational demand of amendments now poses a material risk to study timelines, site participation, and trial efficiency.

This summary synthesizes direct feedback from site leaders responsible for regulatory affairs, finance, coverage analysis, and clinical operations. The findings reflect real-world execution challenges and practical recommendations to improve amendment performance without compromising regulatory rigor or patient safety.

KEY OBSERVATIONS FROM SITES

1. **Communication breakdowns, not regulatory complexity, drive most amendment delays**

   Sites consistently reported receiving notice that an amendment exists without receiving:

   - The **full** amendment packet to allow processing
   - A clear summary of what changed and the priority for implementation (e.g., if patient safety relevant with modification priority would be high)
   - Budget or coverage-related documentation

   In many cases, central IRB approval occurs before sites are operationally or financially equipped to implement the amendment.

2. **Budget template delays are the single largest bottleneck**

   Across institutions; sites reported waiting weeks or months for updated budget templates.

   During this time:

   - Coverage analysis and MCA updates cannot be finalized
   - CTMS calendars cannot be confidently released

   Sites operate "at risk" to maintain compliance and patient continuity

3. **Sites are absorbing risk to keep trials moving**

   To avoid patient impact or compliance gaps, sites described:

   - Implementing amendments immediately after IRB approval, before contracts are finalized
   - Creating interim calendars or bill holds
   - Billing conservatively to research and reconciling later
   - Holding accrual or monitoring visits to force sponsor engagement

   These practices keep trials running but shift operational and financial risk downstream to sites.

4. **Amendment performance influences site participation decisions**

   Multiple leaders shared that prolonged amendment delays have resulted in:

   - Closing accrual
   - Withdrawing from studies
   - Declining future studies from the same sponsor

   Amendment execution is now a site selection and retention factor, not just an operational detail.

WHAT SITES ARE ASKING SPONSORS TO DO DIFFERENTLY

Sites emphasized that they are not asking for perfection, but for predictability, completeness, and early visibility. Specific, actionable sponsor-side improvements include:

- Providing a one-page amendment impact summary
- Delivering budget templates concurrently with amendment packets
- Offering early notice of pending amendments, not just waiting for IRB submission acknowledgments
- Identifying clear escalation contacts with the Sponsor when negotiations stall or delays in a full amendment packet occur
- Aligning on realistic site timelines and internal dependencies (ensuring priority for both Sponsor/CRO and Site so that resourcing can be intentionally planned)

These changes are viewed as low-burden for sponsors and high-impact for sites.

WHY THIS MATTERS TO SPONSORS

Improving amendment execution:

- Reduces downstream delays and rework
- Improves site trust and engagement
- Preserves enrollment momentum
- Lowers the risk of site attrition
- Supports faster, more predictable trial delivery

Sponsors that treat amendments as an operational partnership rather than a transactional update will be better positioned to compete for high-performing sites.

Ready to help your sites keep studies moving?

Connect with WCG to support smoother site execution and enable greater study success.