Best Practices for Study Startup

Site Enablement League

Budgets Working Group

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About this document

The clinical trial startup process is complex and involves many stakeholders. This document provides best practice recommendations for Study Startup Collaboration from the Budgets Working Group of the Site Enablement League. By implementing these best practices, stakeholders can improve startup success rates, reduce timelines, and enhance overall trial efficiency.

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Introduction

The startup phase of a study at a clinical trial site is lengthy and can be frustrating for all stakeholders. There are many processes that must happen for startup to be complete, and delays occur in almost all phases with regular irregularity. Many stakeholders have the goal of standardizing the process, but every sponsor, study, and clinical trial site has its own requirements, meaning that each study start at every clinical trial site can be unique. Furthermore, the staff working on study startup have a wide range of experience and expertise, which further contributes to the uniqueness and complexity of study startup.

Budget negotiation is a key part of study startup at a clinical trial site, and the focus of this working group. However, the budget negotiation process has dependencies and an impact on many of the other tasks that happen during study startup. The working group noted that there is often a lack of understanding of this interdependency, and in general about the many tasks that happen at a clinical trial site during startup. All stakeholders in the industry could benefit from understanding this process. Before assessing how to improve the budget process the working group identified high level study startup tasks and then focused on the budget negotiation process to highlight the importance of understanding the holistic process.

The goal of this document is to educate all stakeholders on the budget negotiation in the study site startup process, identify common pitfalls, and suggest best practices for improving the process. If all stakeholders understand each other's perspectives, improving transparency in the process, then collaboration can be improved.

General Site Startup Tasks

This is a generalized list of tasks a clinical trial site must complete during study startup, **in no particular order**:

- Committee approvals
  - These are site-specific, with site-specific rules for order, timing and dependency on/gatekeeping of other processes
  - Some examples are: Radiation Safety, Research Review, Research Oversight
- Informed Consent Form review and updates
  - Determine who needs to be involved in the review and negotiation, communicate with other departments as needed
  - Ex: Budget office, contract team, legal office, etc.

- IT Security review for any technology vendors provided by the sponsor/CRO
- Site Initiation Visit (SIV)
    - Schedule the SIV depending on the study startup progress, factoring in any required stagegates per SOPs (ex: CTA must be signed before SIV)
    - Coordinate space and logistics for all attendees
    - Ensure key personnel are available for the required time
- Training
    - Manage training requirements for all staff, including device/drug training, technology system training, protocol training, etc.
- Ongoing feasibility review
    - Sites should reassess their responses to the feasibility questionnaire during startup, evaluating potential patient volumes, study timelines, ongoing physician interest, new protocol info, coverage analysis, etc. in order to determine if their initial assessment is still valid and startup should continue
- Contract Negotiation
    - Determine who needs to be involved in the review and negotiation, communicate with other departments as needed (ex: outsourced legal, corporate legal, etc.)
- Internal system setup
    - Configure any technical systems that must be used for the study
    - Ex: CTMS, IRB, Patient payments, etc.
- System access
    - Manage all study staff system access requests for sponsor/CRO-provided systems (EDC, ePRO, IRT, etc.)
    - Manage all study staff system access to all site-owned systems (CTMS, eReg, payments, IP management, etc.), including ensuring required training is complete, requesting/granting access, ensuring appropriate roles/permissions are assigned
    - Ensure system access is discontinued as staff leave or stop working on a study
    - Manage CRA/monitor access to site-owned systems (EHR, eReg, etc.)
- IRB approval
    - Determine the IRB of record (internal vs. central, or both)
    - Clarify the responsibility of each party (sponsor, CRO, site) in the submission process

- Manage the IRB process, collecting all documents and ensuring they are submitted appropriately, informing key stakeholders of the IRB board date, ensuring the PI is available to present/answer questions as needed, relaying the decision to all key stakeholders, collaborating on any required changes, sending all approved documents to the appropriate parties (ex: CRO, sponsor, monitor, staff, etc.)

- Regulatory document submission
  - Understand the expected document list
  - Manage expected document completion for all study staff
  - Collect and submit all expected documents to the sponsor/CRO
- Fraud prevention assessment and process creation
  - Ensure that a process exists for preventing participant fraud
- Medicare Coverage Analysis (MCA)
  - Determine whether protocol-required tasks/activities will be paid for by the sponsor or billed to insurance by evaluating whether each medical service, device, drug, or procedure meets the criteria for reimbursement under **Medicare and Medicaid**. This process determines if the item or service is "reasonable and necessary" for patient care based on **clinical evidence, safety, effectiveness, and cost considerations.**
- Billing and payments setup
  - Internal finance system setup/review/oversight as needed depending on the drug/device and study type, including drug/device pricing and billing codes
- Budget Negotiation
- Hospital service assessment
  - Determine the protocol tasks that require procedure and testing service and staffing needs from the hospital
- Laboratory service assessment
  - Determine the protocol tasks that require laboratory services (local or central), including logistics such as sample transportation or shipping, specific sample handling, etc.
- Operational logistics assessment
  - Determine the protocol tasks that require staff effort, facility space, or other logistical support (ex: drug storage, handling, etc.)
- Hospital service implementation

    - Coordinate with hospital departments and staff to explain protocol requirements and agree on workflows needed to complete protocol tasks per the hospital service assessment completed during startup
- Device/drug/supply shipping logistics
    - Ensure storage facilities meet all requirements (Ex: secure, temperature controlled, etc.)
    - Ensure shipping addresses are correct in all systems of record
    - Coordinate the process for receiving shipments
    - Create the system/process/tool for accountability record keeping
    - Create the system/process/tool for tracking inventory levels, expiration dates, and resupply triggers

Each site will have a unique process for completing all of these tasks during study startup. At some sites, many of these startup processes may be managed by unique and independent teams, and so it is important to identify the dependencies between processes and ensure those are planned for. This paper will use the budget process to demonstrate how understanding such interconnectivity can prevent startup delays.

The Site Startup Workflow

The exact process of the startup workflow depends on things such as:

- Organizational structure of the teams involved
    - Ex: Is there a central clinical trials office that manages the CTA or does the lead research coordinator handle these negotiations
    - Is there a dedicated regulatory team or does the lead research coordinator manage the submission
    - Are there multiple departments involved in this study, or are there multiple facilities participating in the study
- Required committee reviews prior to startup beginning (order and dependencies)
    - These are site-specific
- Required order of operations of startup tasks, as documented in the site Standard Operating Procedures (SOPs)
    - Ex: Some sites require a committee review before any startup tasks can begin
    - Ex: Some sites require the CTA to be in final approved status before they will submit to IRB
    - Ex: Budget finalized prior to CTA review

- Personnel involved in each task
  - Personnel from multiple departments may need to be informed, involved, and/or trained
- Systems used for each task
  - Multiple systems may be used for the startup process, and the workflow depends on if those systems are site-owned vs. sponsor/CRO-provided

The Study Budget Process during Startup

Budget negotiation during startup is not a process that can occur in isolation. The Clinical Trial Agreement (CTA) includes both the budget and the contract. These are often negotiated by different teams, yet they are interconnected and must be aligned. Successful completion of the CTA also relies on coordination with the teams responsible for IRB submission, MCA, and operationalizing the clinical trial activities. This cross-departmental coordination can be difficult depending on the organizational structure and team member responsibilities. At a small site, one or just a few people might be managing all of these processes, but at a large site or site network this work might span many departments and locations. Here we take a closer look at the startup item of “Budget Negotiation” from the general startup activity list in order to highlight the complexity and dependency on other startup processes.

Detailed budget negotiation process:

- Receive budget template or portal invite from sponsor or CRO
  - Request editable document (if locked)
  - Log into portal to view budget template
  - Send to or manage access for any other personnel who need to review
- Determine if a Master Service Agreement (MSA) exists with this party/parties
- Determine past studies conducted with this party/parties and gather past budgets as a reference for this negotiation
- Request an introduction call with the Sponsor/CRO
  - Determine the correct points of contact for questions and escalations
  - Establish expectations for communications and response times
- Ensure receipt of or request final protocol and all supporting documents (lab manuals, pharmacy manuals, vendor manuals, etc.) to ensure all clinical trial activities are planned for and adequately captured in the budget

- WAIT for all supporting materials before starting in order to optimize the budget review
- Add overhead and standard institutional costs (with justification language) if not already included in an MSA
    - Examples include: Startup fee, Remote monitoring visit fees, IRB renewal fees, CRA turnover fees, technology platform fees, etc.

POTENTIAL DECISION POINT:

- Consider sending the budget with overhead and standard institutional costs to the sponsor first for initial review before putting more effort into the negotiation, especially if this is the first time working with these parties and/or if something has dramatically changed since the last study

Continue if overhead and standard costs are agreeable to sponsor/CRO:

- Receive and review protocol and all supporting documents (lab manuals, pharmacy manuals, vendor manuals, etc.) to ensure all clinical trial activities are captured in the budget
    - Review budget template and add specific details and activities to any generic budget line items (ex: "Screening Visit" expands to "Screening visit activities: Blood draw, consent discussion, screening questionnaire", etc.)
    - Add any missing budget line items for required protocol activities (ex: setup or direct cost of required software for protocol activity, ex: both hospital and professional charges for a required scan, etc.)
    - See the Best Practices for Budget Estimations document for a deep dive on how to conduct this process
- Build Medicare Coverage Analysis (MCA)
    - This provides the starting point for subject-related costs that need to be included in the budget
- Identify site stakeholders who will need to determine required resources and staff effort and to conduct the cost analysis for each budget line item. This list will be site dependent, but some examples are:
    - Hospital staff for procedures/scans
    - Research clinic staff or outpatient clinic staff for follow-up visits
    - Lab staff for sample handling
    - Pharmacy staff for drug handling

    - Note: consider standardizing this information with those departments to streamline future negotiations
- Work with stakeholders to review and assess the ACTUAL research staff time and effort required for procedures and protocol activities and include that effort as a budget amount (based on the FTE salary for the type of staff member and time estimates)
    - Explain the effort required to realistically complete tasks in compliance with all regulations and protocol requirements
    - See the Best Practices for Budget Estimations document for a deep dive on how to conduct this process
- Attach justification for all standard costs and changes to the budget template
    - See the Best Practices for Budget Justifications document for details on this process
    - Specify what is non-negotiable
    - Consider creating a standard institutional document with these details
- Ensure startup document congruency
    - Collaborate with regulatory staff to ensure any patient time estimates, costs, reimbursements, etc. are included and match in both the budget and the ICF
    - Collaborate with the contract negotiation team to ensure that contract payment terms found in CTA are reflected in the budget
        - Ex: Interest charges for delayed payments
        - Ex: Non-payment terms for startup payment
- Ensure operational congruency
    - Collaborate with the legal and clinical operations staff to ensure operational language in the protocol, contract and budget are aligned and acceptable
        - Ex: Witholding 10% of payment until data closeout - does this have implications for clinical trial staff that are unacceptable?
        - Ex: Screen failure rate and screen failure payment limits - will this cover the expected effort required to enroll the expected number of participants?
- Submit!

Wait for a response

- Track response time and follow up if needed, in alignment with response time expectations set in the introductory call
- Evaluate negotiation responses
- Request a call for items that are difficult to negotiate

  - Requesting a call can significantly decrease the negotiation time, avoiding multiple back and forth emails with time spent waiting for a response
- Escalate to the sponsor if there is a CRO involved and there is a delay in response times
- Finalize the budget

Common Pain Points

The budget process continues to be a painful part of the startup process. WCG survey data shows that budget negotiation times have not improved in the past four years and that proposed budgets continue to be significantly lower than the final negotiated budgets (*www.wcgclinical.com/insights/clinical-trial-budgets-current-trends-questions-answered-part-1/*). Common pain points heard across the industry are:

- Lengthy back and forth negotiations over email waste a lot of time
- Low proposed budgets waste a lot of time by increasing the number of "turns" or negotiation cycles
- Lack of justification language to support budget additions and changes makes it difficult to approve site requests
- Lack of alignment with operational teams on the specific protocol tasks and effort needed for those tasks puts sites at risk for losing money or having to renegotiate the budget when the team realizes the misalignment
- Less experienced budget negotiators may be more likely to accept the proposed budget and therefore are at risk for losing money during a clinical trial

Secrets for Success

Reviewing the process outlined here is a starting point for success. Many teams are not aware of all the steps that should be taken during the negotiation. Furthermore, the SEL members share these tips that have been particularly helpful:

- Understand where alignment is needed between departments and ensure that happens early to avoid rework
- Focus on a process flow and understand where individual workflows can occur in parallel and where dependencies exist
- Set clear expectations early - a phone call can improve alignment significantly
- See the Best Practices for Budget Estimations document for tips on how to establish a standardized rate/justification document to share with sponsors/CROs

  - Clear and early communication of site non-negotiables can avoid wasted time later
  - Review rate cards annually and update based on operational, institutional or facility changes
- Build an internal "Playbook" for your budget item base and ceiling rates to facilitate negotiations
- Ensure that ANY protocol changes made after the CTA is signed get flagged for review to ensure no budget updates are needed

Controversial Suggestions that would Advance the Industry

Although there is common agreement on the frustrations and challenges of budget negotiations, there is no alignment on potential solutions. If the budget process was faster clinical trial timelines would be faster. Can we balance the delays caused by the current process with the "savings" the process produces? Can we accept slightly less savings for increased speed? The working group members suggest these radical ideas that would have a dramatic impact on the process:

- Sponsors/CROs: Use a higher starting point for site budgets
  - Evaluate past study budget starting points, final agreements and the number of negotiation cycles to understand the landscape
  - Consider if a slightly higher starting budget would result in less negotiate cycles and therefore faster startup
- Sponsors/CROs: Be more flexible with number of turns required before approving an increase or escalating the request from the CRO to the sponsor
  - Too many playbooks require a stifling number of negotiation cycles before an escalation or approval - this is a waste of time
- Sponsors: Give CROs a broader negotiating band so they can negotiate faster with sites
- Sites: Use software to help ensure you are capturing all required protocol tasks in your budget line items and to understand fair market value rates for those tasks
  - Newcomer vendor recommendations: Upsite Clinical, SiraSite