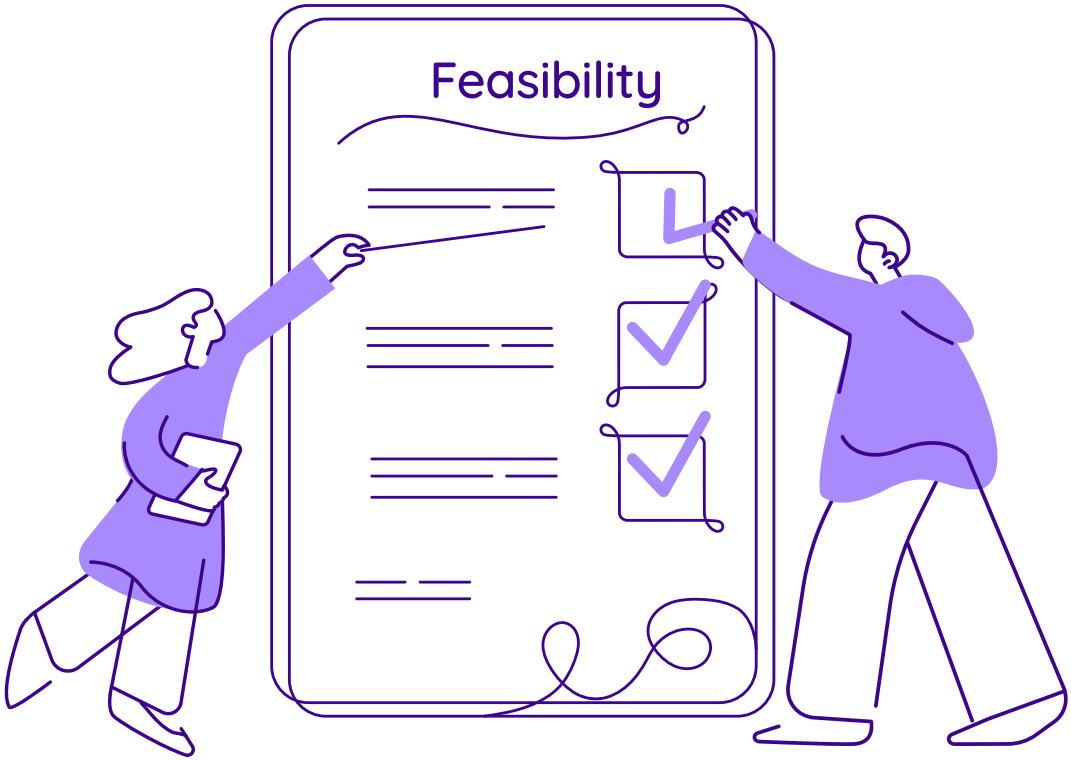
A Site Enablement League Whitepaper



Redefining Feasibility in Clinical Trials

Collaborative Approaches for Improved Site Selection

A whitepaper by Working Group A: a group of senior executives from sites, sponsors, and CROs who collaborate to design the future of how stakeholders work together through technology to advance cures.

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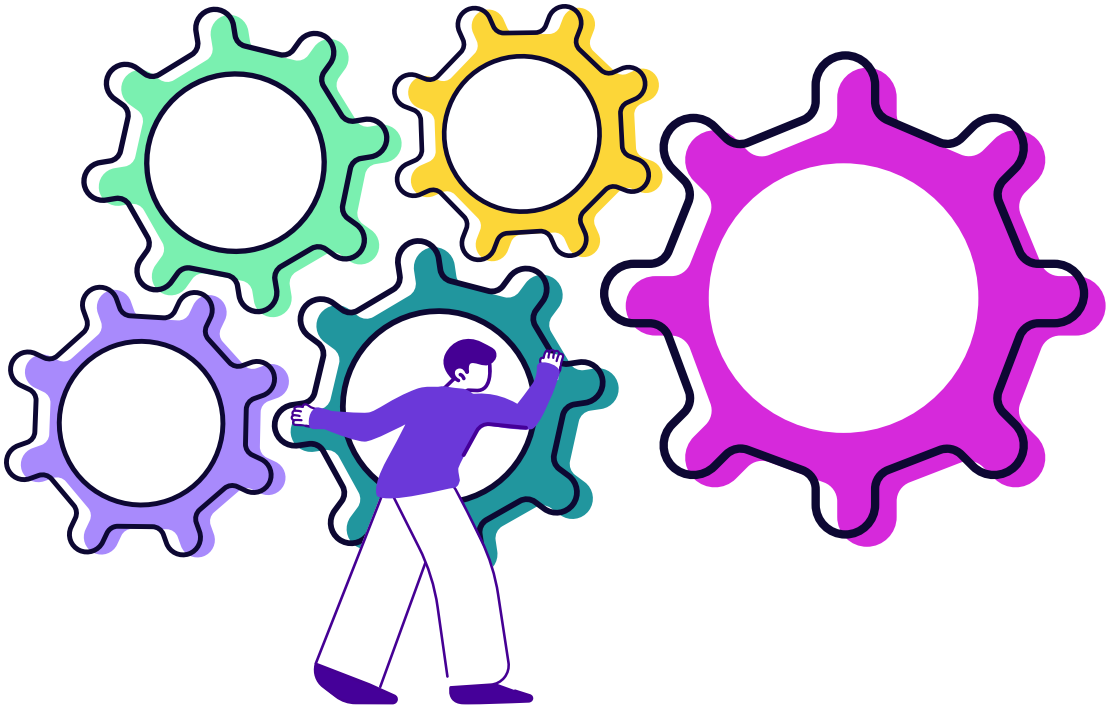

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Executive Overview

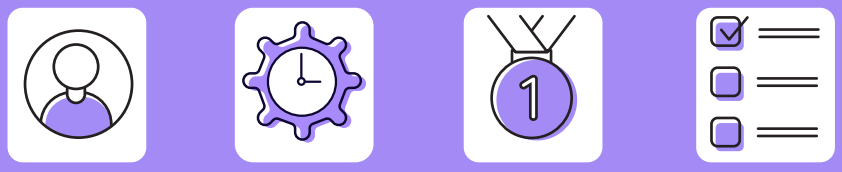
This white paper by the Site Enablement Working Group on Feasibility dissects the intricate nature of 'feasibility' in clinical trials, with an objective to recast it through mutual understanding of challenges, bolstered collaboration, and transparency among sponsors, CROs, and sites.

The paper confirms a significant gap in the industry's process for Site Feasibility and underscores the pressing issues identified by the American Society of Cancer Oncology (ASCO) Task Force survey. It emphasizes the need for better differentiation between the three main stages of feasibility: Program, Study/Protocol, and Site Feasibility, and the four sub-phases of Site Feasibility: Profile, Capability, Performance and Protocol-Specific assessments.

Feasibility Stages:

1. Program
2. Study/Protocol
3. Site Feasibility

Feasibility Sub-phases:



Profile | Capability | Preformance | Protocol-Specific Assessments

It also highlights known key challenges, and most importantly, emerging trends like early initiation of Site Feasibility and premature engagement of sites by Contract Research Organizations (CROs). To fully explain these challenges, the paper analyzes the current practices and their downstream impact on clinical trial execution for all stakeholders. A list of best practices emerges naturally from this analysis. These findings are aggregated into a short and actionable best practices guide for site feasibility, with useful references to explain the rationale.

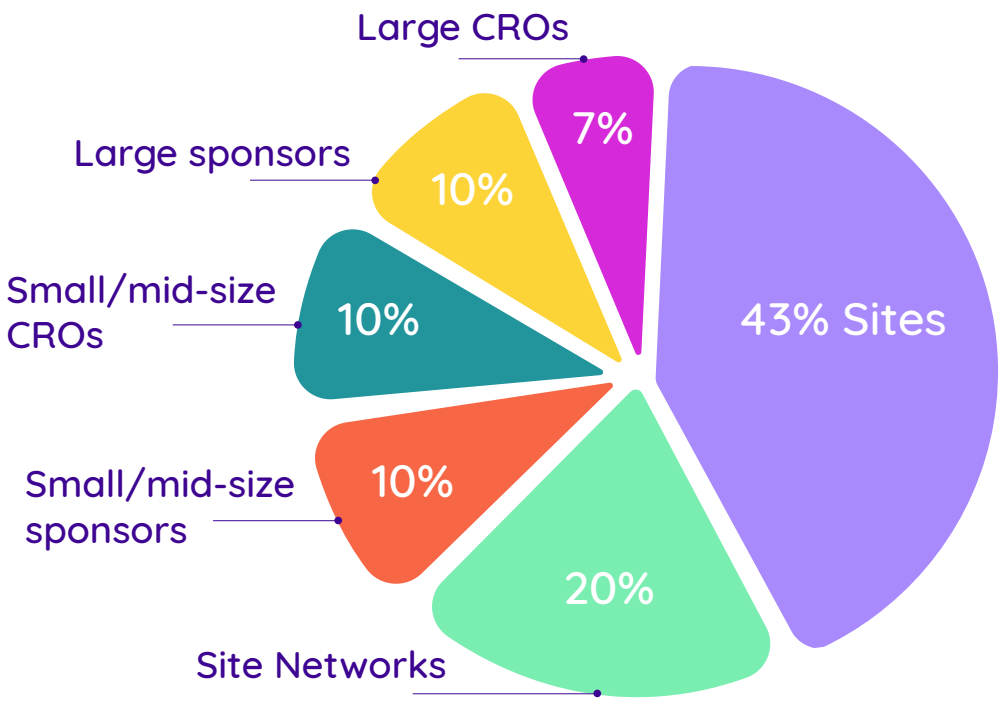
In conclusion, the paper urges the industry to actively address these issues by implementing practical solutions. It advocates for industry-wide collaboration, data standardization, redundancy reduction, and automation tools, while acknowledging that these changes necessitate broader industry transformation. The potential benefits of evolving this process are significant and meaningful for more efficient and successful clinical trials.

Introduction

The Working Group

The Site Enablement League is focused on streamlining processes, implementing advanced technologies, and fostering effective communication among all industry stakeholders to create a more agile and innovative clinical research environment, leading to faster development of life-saving treatments. The Site Enablement League Working Group on Feasibility was convened to bring focus and collaboration to improving the process of site feasibility. The group was composed of representatives from sponsors, CROs and sites (43% Sites, 20% Site Networks, 10% Small/mid-size sponsors, 10% Small/mid-size CROs, 10% Large sponsors, 7% Large CROs). The broad representation of the working group increases the group's potential to identify newly emerging challenges, increase awareness of the challenges each party faces, and formulate practical recommendations for improvement.

The Site Enablement League Working Group



Introduction, cont'd

Defining the Problem

When discussing feasibility, it is important to first define the scope of the problem. The concept of "feasibility" in clinical trials is multifaceted, encompassing three stages of the clinical trial process .

1. **Program Feasibility** - This involves assessing disease prevalence, competitive landscape, regulatory norms, and geographical aspects to craft a trial program.

2. **Study/Protocol Feasibility** - This includes evaluating clinical, technical, regulatory, geographic, and operational components of a particular protocol to ensure optimal project completion concerning timelines, targets, and costs.

3. **Site Feasibility** - This entails identifying and assessing potential sites for a specific study. The working group determined that the feasibility assessment can be further segmented into four areas:
    - Site Profile Information - basic site information such as address, specialty areas, number of physicians, startup process, review committees required, etc.
    - Site Capability information - what equipment does the site have and what lab tests can be performed.
    - Site Performance information - enrollment performance to target, inspection findings, data quality metrics, etc.
    - Specific protocol assessments - patient population estimates, referral patterns for the disease state, standard of care (SOC) details for the disease state in question, ability to conduct specialized procedures or tests, etc.

Introduction, cont'd

A limited number of industry professionals participate in all three stages, causing the term "feasibility" to hold a unique meaning to each individual involved in the clinical trials process. Thus, when working with a cross-functional, cross-organizational group, it becomes crucial to clarify the process under discussion.

Many of the recent conference discussions and industry working groups about improving feasibility concentrate on operational improvements in the initial two stages, paying little attention to the third stage of feasibility, Site Feasibility. However, conversations with clinical researchers suggest a notable frustration regarding the site feasibility process and an apparent lack of awareness of site challenges at the sponsor/CRO level. There hasn't been a significant change to the process for some time, with recent minor "innovations" at the sponsor/CRO level actually creating additional site burden. Furthermore, sponsors only occasionally solicit or receive site feedback, leaving sites reluctant to respond or to provide candid feedback to avoid straining their relationships with sponsors. For sponsors and CROs, the necessity to select qualified sites (required by federal regulations such as 21CFR312.53 and 21CFR812.43) and the risk of inspection findings on the process of site selection can deter stakeholders from making changes to the process.

Site Feasibility Challenges

The major challenges faced during site feasibility are well-recognized among sites and are often a topic of discussion among clinical researchers. The American Society of Cancer Oncology Task Force recently released survey results summarizing commonly understood but poorly documented issues with site feasibility for oncology sites and highlighting the scale of the challenge. The results offer a quantitative measure of the problem's scale and impact in oncology. The results are applicable across all therapeutic areas, and therefore the scale of the problem across the industry is estimated at $1.6B [Clinical Leader].

Methods

The ASCO paper suggested that the industry could, and should, instigate process changes to streamline and standardize the site feasibility process and leverage technology to support the process. The Avoca Quality Consortium (AQC) recently partnered with ASCO to develop a new site feasibility suite of tools, including standard profiles, feasibility forms and checklists that are simple, effective, standardized with minor adaptability, and flexible enough for sites.

Both AQC and ASCO acknowledge that standardization requires collaboration between all stakeholders, and lack of buy-in from sponsors and CROs is a major barrier to change. These new tools may be the catalyst for collaboration between stakeholders.

For any sustained change, the industry must develop a shared comprehension of the problem. The goals of the working group were to identify problems in the process that might be new or unknown to all stakeholders, to raise awareness of those issues, and to identify potential solutions.

1. **Scope:** The working group first defined the scope of the project and agreed on the definition of Site Feasibility.

2. **Review:** They reviewed the available literature on the issue.

3. **Subgroups:** Next, they were divided into sub-groups of sites and sponsors/CROs to discuss current site feasibility processes and the challenges they experience with those processes.

4. **Independent Review:** The sub-groups explored these questions independently so that all points of view would be represented in the group discussions.

5. **Desired Outcomes:** Each group also suggested desired outcomes from the working group.

6. **Discussion:** The sub-groups reconvened and discussed the current processes first. Next, the group spent time discussing the challenges identified by each group. There was idea sharing between people in the same sub-group, and information sharing across sub-groups. As the challenges were discussed, some challenges were identified that not everyone in the working group was aware of.

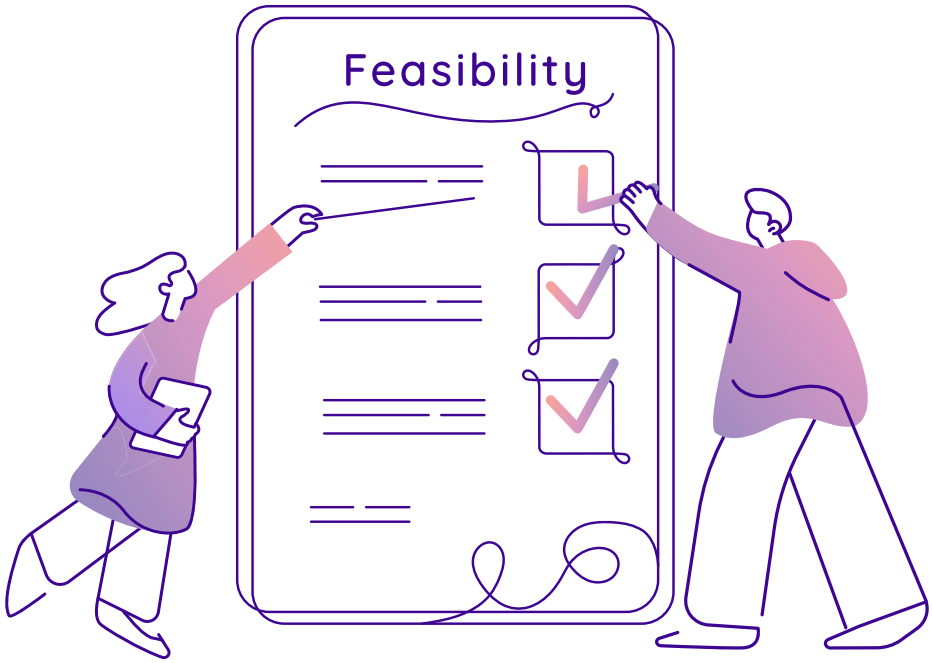
Methods

Finally, the group aligned on the desired outputs, recognizing that it was important to share this information with the industry. The unique composition of this group will lead to a balanced perspective and output applicable to all stakeholders.

A collective goal that emerged was to create standards for data collection and to design an automation tool to reduce redundancy in the process. While this idea was appealing, it would necessitate a technical solution and process change for all stakeholders, which is beyond the reach of a working group.

A more attainable goal was to raise awareness of these new trends and share best practices to handle the associated challenges. They committed to dissecting the challenges to identify the root causes and risks to all parties. By identifying root causes and risks they were also able to suggest best practices for avoiding these challenges. Since these challenges have an impact on both “sides” of the industry, sites as well as Sponsors/CROs, the group agreed this was valuable. The challenges, root causes and risks are presented here to help inform and drive change. Raising awareness now could minimize the impact of these trends or alter the trends in a meaningful way.

Finally, the group developed a checklist to help implement the best practices recommended here.



Findings

Three Emerging Challenges in Feasibility Identified

As anticipated, the group cited numerous examples of challenges referenced in the ASCO paper, namely redundancy and lack of standardization, which result in inefficiency such that the process consumes valuable site resources. Three unexpected findings also arose from the discussion: (1) early initiation of site feasibility, (2) the emergence of CROs engaging sites in pre-award feasibility, and (3) ineffective communication between Sponsors, CROs, and sites. From the sites' perspective, these trends are either newly emerging or worsening, and are leading to subsequent disruptions and significant delays during startup. Amongst the sponsor and CRO participants, there was mixed awareness of these trends and their consequences.

We will discuss these new findings here, noting that there is a wide variability in the size, available resources, and experience of Sponsors, CROs and sites, as well as across therapy areas and disease states. This variability means that not all findings will apply to all groups; nevertheless, it is important to share trends observed in the industry before they become widespread.

Three Emerging Challenges:

1. Early Initiation of Site Feasibility
2. Premature Engagement of Sites
3. Timely Communication

Challenge 1: Early Initiation

Early Initiation of Site Feasibility: Implications and Unforeseen Consequences

A newly observed trend highlighted in the discussions suggests that the Site Feasibility process is being initiated earlier for two primary purposes: to utilize site feedback for finalizing Study/ Protocol Feasibility and to expedite the time to First Patient In (FPI).

In the first scenario, sponsors are effectively engaging the earliest potential sites, typically experienced research centers and/or sites with Key Opinion Leaders (KOLs), to gain insights for Protocol Optimization. The feasibility evaluations serve as a conduit to refine the protocol based on the input from these sites regarding aspects like procedure requirements, treatment details, inclusion/exclusion criteria, and participant burden. This feedback is obtained through queries from the site and/or discussions with the site and PI during the feasibility phase or at the site visit (Pre-selection site visit/Site qualification visit).

In the latter scenario, Sponsors and CROs aim to reduce study timelines by reaching FPI more rapidly. A primary step towards this goal involves quicker identification and selection of sites. Given that many sponsors frequently collaborate with the same sites, it may seem obvious to begin the feasibility process as early as possible. However, Site Feasibility is often beginning before all the protocol, lab, and vendor specifics are finalized.

In both situations, the lack of precise details and/or the subsequent additions/changes to the protocol and supporting documents can invalidate a site's responses to the feasibility questions. For example, specific requirements and details about sample processing, storage necessities, central lab locations, vendor requirements, and equipment often determine a site's capability to participate or involve satellite facilities. When such details emerge much later during startup, sites might be unable to comply with the requirements or may need to revise IRB approvals, budgets, contracts, and facility plans.

This is often not discovered until after selection, or even as late as at the Site Initiation Visit, and can dramatically impact a site's ability to participate in the study. In many cases, the result is disruptions and delays during the startup phase. Unknown unknowns about protocol details cannot be accounted for during feasibility; transparency about such uncertainties should be shared in a timely manner to avoid negative impacts. The group noted that this does not happen with all Sponsors and CROs and not all sites are targeted for this earlier feasibility process.

*Key Finding: Many sites are either unacquainted with this trend or have not experienced it yet, and the potential impact remains unnoticed by sponsors/CROs, or is attributed to site startup delays rather than a systemic problem with the feasibility process.

Challenge 2: Premature Engagement

Premature Engagement of Sites in Feasibility Process by CROs

Another challenge identified by the group is the practice of CROs initiating the Site Feasibility process even before securing the study contract from the sponsor. This process may be driven by the desire to have a ready set of highly qualified sites to present to the sponsor as part of their bid for the study. Alternatively, it serves to jumpstart the site selection process at the earliest possible moment once the study has been officially awarded.

Under such circumstances, sites often find themselves involved in what appears to be a normal feasibility process, with no awareness of the additional layer of uncertainty. Sites are not typically told that they are only getting partial protocol information. They may be unaware that the opportunity for the study itself is far from certain, as the contract has yet to be awarded to the CRO. This preemptive engagement with sites is a considerable commitment of resources and time for both sites and CROs, leading to waste if the contract is not awarded, and inaccuracies in the long run due to incomplete protocol information.

Interestingly, this emerging trend seems to have flown under the radar for most sites and sponsors. It is imperative to bring this to the attention of all involved parties to prompt a reevaluation of current practices and to mitigate any adverse effects on the feasibility process.

*Key Finding: Some sites and sponsors appear to be unaware that this is taking place, suggesting a lack of communication and transparency within the current system.

Challenge 3: Timely Communication

The Crucial Role of Clear and Timely Communication

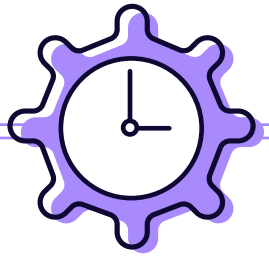
Effective communication sits at the heart of a successful feasibility process. However, the occurrence of unclear or delayed communication, or difficulties in bridging gaps between different parties, can substantially hinder the process. Critical information about realistic timelines, desired milestones, actual statuses, knowns and unknowns is paramount to effective resource optimization at sponsors, CROs and sites. This impacts appropriate staff allocation, scheduling of study activities, and an accurate understanding of the study pipeline and portfolio to ensure reliable commitments to study enrollment numbers.

Interestingly, this issue impacts all parties in the process. If sponsors or CROs are not sharing crucial information then sites and/or CROs can't be confident in their resource planning. If sites are not transparent about their timelines or don't offer highly accurate responses to enrollment planning questions, then sponsors and CROs can't allocate resources appropriately. Tackling this tri-directional challenge is paramount to making progress in the industry.

The discussion in the working group indicated a consensus that these communication-related challenges tend to be amplified when all three parties - the Sponsor, CRO, and Site - are involved. The potential for miscommunication or misunderstanding increases with each additional participant, necessitating a deliberate and coordinated approach to communication.

To illustrate, consider the area of transparency in site selection: Sites often express a desire for clear and honest feedback regarding their non-selection for a specific study. Having a transparent understanding of the reasons behind their exclusion can empower sites to improve their performance and enhance their prospects for future participation. However, this valuable insight can only be gained through open, honest, and timely communication from the sponsors and CROs.

*Key Finding: The lack of clear and timely communication can adversely affect the feasibility process, leading to inaccurate commitments, resource misallocation, and overall inefficiencies in the trial process.



Discussion: Impact of Current Feasibility

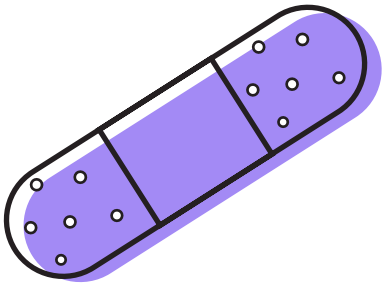
Impact of Current Feasibility Processes and Best Practices to Mitigate Risk

A clear recommendation from the working group is that clear boundaries should be set between Study/Protocol Feasibility and Site Feasibility. There was clear agreement that sites should be engaged in the Study/Protocol Feasibility process. This recommendation is specifically stated in section 3.1.3 of the recently updated ICH Harmonised Guideline for Good Clinical Practice as part of the Trial Design process, and is also mentioned in the CTTI Quality By Design document. This feedback should not occur during the Site Feasibility process.

Input from sites should occur during protocol design via an early stakeholder engagement framework and should include operational and scientific feedback. The operational details of the protocol are often overlooked and many assumptions are made about the ability to conduct protocols. Sites are eager and willing to consult on operational details of protocol design because they want protocols that are clinically reasonable and operationally viable. In order for their feedback to be actionable, sites need to be engaged earlier in the protocol writing process. Furthermore, the working group consensus was that protocol feedback should be a paid consulting opportunity.

Creating clear separation between the two phases, or at least being transparent about the stages of the process will prevent delays and disruptions. Transparency throughout the process, from all stakeholders, is critical to success. If critical details are not yet finalized when the site feasibility process begins, and the site is not informed, it could have a significant downstream impact.

A second observation of the working group is that the Site Feasibility process should also be divided into phases (identified in the introduction). Sponsors should consider separating these phases as ways of engaging with sites sooner without impacting startup and recruitment timelines later. For example, by collecting site profile, capability and performance data, which is unlikely to change much in a short time period, early in the process, they can engage sites and start the process before the protocol is finalized. It would be even more ideal to have real-time access to current site profiles and capability data from a large number of sites.



Discussion, cont'd.

The Shared Investigator Platform (SIP) was intended to provide this functionality, but in the working group's experience this has not materialized. By having this profile and capability data, sponsors can identify a more targeted list of sites to engage for the third phase, protocol-specific assessments. With a targeted list of sites and real-time/current data on capabilities and performance, Sponsors/CROs would also be able to reduce the questions asked to sites, streamlining communication, reducing redundant work, and focusing on the critical details required for sites to make an accurate assessment of their ability to execute a protocol. The industry is taking the steps to develop tools that can more effectively facilitate the process and need to be more widely and uniformly adopted not only by sites but used by CROs and sponsors to create a basis for further improvements.

To get to this ideal state, stakeholders must understand the impact and risks of the current processes. Currently Study Feasibility and all phases of Site Feasibility are overlapping. To help stakeholders understand the implications of these current dynamics, a list of trending actions and critical path items, as well as the associated impacts of proceeding with Site Feasibility under those conditions was developed (Table 1). The overarching impact is that steps that are taken to speed these processes up often result in sites being unable to confirm they have interest in the protocol, the target patient population, or the resources (people, facility, equipment, capabilities) to successfully support the trial. Often this information is not provided until much later in study startup. The downstream impact of this missing information is that sites are unable to accurately complete budget development processes (determine all the costs, qualifying clinical trial (QCT) determination, then either Medicare coverage analysis (MCA) or study reconciliation) and negotiate a budget fair to all parties, including the subjects. Of note, many best practice recommendations suggest sending the draft version of an item. This was a compromise in the working group to agree that at least receiving the draft is better than not receiving anything, and lets sites proceed with a little more confidence in answering feasibility questions. It should be clear, however, that sites can only respond based on the provided information. A draft/synopsis is not always enough to ensure an accurate site feasibility response.

Table 1.

List of Trending Actions and Their Impact on Site Feasibility

Action/Item	Reason/Rationale	Impact	Best Practice
The full protocol is not sent until after selection; sites only receive slides or synopsis during feasibility.	Possible reasons: Protocol is not yet finalized but starting site feasibility to decrease time to FPI. May be seeking input from experienced sites for protocol optimization; are willing to make protocol changes early in process (Especially true with smaller sponsors).	Sites are unable to make an informed decision on participation, provide accurate enrollment projections, determine compliance with standard of care treatment expectations, or determine if they have the resources available to meet all protocol requirements. Sites can't determine whether community or satellite locations can participate. Sites can only respond based on the provided information. A draft/synopsis is only valuable to determine initial site interest, not accurate site feasibility.	Site Feasibility should begin after the protocol is finalized or close to finalized. The full/ final protocol, or a full draft or detailed synopsis to include mechanism of action (MOA), if applicable, and inclusion/ exclusion (I/E) criteria as well as schedule of activities (SOA) should be shared.
Inclusion/Exclusion criteria are not finalized.	The protocol is not finalized but sponsors/ CROs expect sites to estimate enrollment based on major I/E criteria to speed up the site selection process.	Sites are unable to accurately project enrollment estimates without knowing all I/E criteria.	Sponsors should finalize I/E criteria prior to site feasibility. The best practice is to leverage early stakeholder engagement to finalize I/E criteria.
Pharmacy manual is not available.	The manual is not finalized and/or the vendor has not been identified or the contract is not finalized.	Sites are unable to determine whether investigational pharmacy services has the resources, staff, or space to handle the investigational drug requirements.	Sponsors should share investigational product handling, stability and resource requirements during feasibility for sites to make an accurate assessment.

Table 1.

List of Trending Actions and Their Impact on Site Feasibility

Action/Item	Reason/ Rationale	Impact	Best Practice
Detailed lab manual or operational requirements are not sent during feasibility (Ex: formulation requirements, sample collection, sample processing, equipment and shipping requirements).	Lab manuals are not finalized and/or vendor contracts are not complete and draft information is not shared. Vendors may be creating the manuals with a timeline for final completion close to FPI. Sub-contracted labs for specialty biomarkers may further delay final lab manual completion.	Sites are unable to accurately assess if they have the personnel, equipment or ability to comply with the protocol requirements. Sites/site networks can't accurately identify which sites or community/satellite sites can participate without knowing the full capabilities required.	Sponsors should send all detailed DRAFT material (sample types, equipment and requirements) during feasibility. Sites should ask for the draft or final manuals to make an accurate assessment of their ability to conduct the protocol. Sponsors/CROs should expect and allow for rapid budget renegotiation of budget if draft materials are not shared.
Detailed information on central labs is not shared during feasibility (Ex: sample shipping details, processing time, results delivery timelines, on-site banking, short-term requirements, etc.). This is especially detrimental if the central labs are involved in eligibility assessments.	Central lab role/ function is not finalized or the vendor contract is not complete.	Sites are unable to plan for and may later struggle to comply with protocol requirements due to lab processing times and shipping constraints they were not aware of, which impacts visit scheduling and staffing requirements. Sponsors may have unrealisticexpectations related to a protocol's schedule of assessments and/or assumed participant decisions. Sponsors/CROs are unable to filter out sites that cannot meet the lab requirements, resulting in unnecessary expenditure of time and effort.	Sponsors/CROs should ENGAGE VENDORS EARLIER. Sponsors/CROs should seek operational feedback from sites (as an early stakeholder engagement activity) to confirm and finalize lab details. All details and vendor contracts should be finalized/executed prior to the initiation of site feasibility. Sponsors/CROs should allow local labs for eligibility assessments. Sponsors/CROs should plan for vendor limitations and include mitigation options in the contract.

Table 1.

List of Trending Actions and Their Impact on Site Feasibility

Action/Item	Reason/Rationale	Impact	Best Practice
Imaging requirements are not shared at the time of feasibility (Ex: required qualification scans, calibration requirements, staff training, healthy volunteer sample scans, etc.).	Imaging manuals are not finalized and/ or vendor contracts are not complete and draft information is not shared.	Sites are not able to accurately assess their timelines to complete the necessary logistics or additional requirements needed to participate (Ex: additional ICF for healthy volunteers).	Sponsors/CROs should send all detailed DRAFT imaging material and communicate pre-activation requirements during feasibility.
Data points to be collected are not all included in the protocol or lab manuals (There are required data points only found in the case reports forms (CRFs))	Sponsor/CRO data science teams add detailed data points during CRF writing, which often occurs later in the process than site feasibility.	Sites cannot assess if they have all the required equipment or processes in place to adhere to the protocol and meet all data collection requirements.	Sponsors/CROs should ensure that ALL data to be collected is mentioned in the protocol or manuals or that draft CRFs are shared
CROs/Sponsors are not transparent about the timeline and status of the study (FDA submission status, protocol completeness, planned amendments, etc).	Desire to select sites as early as possible to decrease timelines, don't want to demotivate or lose sites when there are delays.	Sites are unable to prioritize their study pipeline and may decline studies they could do later or accept studies that end up competing with others due to unclear timelines. Sites work on feasibility at the risk of the study not being approved by the FDA. CROs are unable to proactively plan the utilization of personnel resources.	Sites should ask Sponsors/CROs about study status. With a list of specific questions, they may be able to gauge the study status to better plan internally and more accurately respond to feasibility questions during the selection process.
CROs/Sponsors are not transparent about enrollment status for studies that are already enrolling.	Enrollment and timelines change quickly and there is not a mechanism to ensure updates are provided during feasibility and startup.	Sites can't accurately estimate enrollment projections and timelines without knowing the current enrollment status of the study and each arm or cohort, as applicable.	Sponsors/CROs should provide regular updates on enrollment to sites in feasibility and startup.

Table 1.

List of Trending Actions and Their Impact on Site Feasibility

Action/Item	Reason/Rationale	Impact	Best Practice
Realistic draft budget is not shared during the feasibility process.	Sponsors/CROs don't want to share too many details with sites before they are selected.	Sites can't determine if there are major budgetary concerns that will cause delays and/or render the study cost-prohibitive during the feasibility process.	Sponsors/CROs should share a draft budget or any major budget constraints/limits prior to site selection.
Sites do not accurately estimate enrollment projections.	Not all sites have good data and tools for estimating enrollment activity. Sites are often basing estimates on only partial protocol information (as mentioned above).	Sponsors/CROs can't effectively gauge participation for the study, leading to inaccurate project timelines, resource needs, and overall cost for all parties.	Sites should be as accurate as possible with enrollment projections, using tools and data to estimate participant populations.
Sponsors/ CROs are not responsive to site questions during feasibility.	CROs cause delays in collecting and asking questions to the sponsor and relaying them to sites. Sites do not always have a clear communication channel to the Sponsor, especially when a CRO is involved.	Sites are delayed in responding or are unable to respond when they can't get timely and accurate responses to questions.	Sponsors/CROs should establish clear communication channels and a plan for timely responses.
Sites are not responsive to Sponsor/ CRO questions during feasibility.	Sites may have staff turnover, may be overwhelmed with study activities, or may decide not to complete the feasibility process. Sites may not be able to address feasibility questions with information as provided by sponsor/CRO or be awaiting responses from supporting service areas.	Sponsors/CROs can't accurately assess potential site lists or plan for startup timelines when sites do not respond. Sites may be replaced by more responsive sites.	Sites should establish clear communication channels and a plan for timely responses. Sites should be clear regrading the reason for delay in answering feasibility questions. Sites should decline if they are not interested.

Table 1.

List of Trending Actions and Their Impact on Site Feasibility

Action/Item	Reason/Rationale	Impact	Best Practice
The feasibility meeting burden on CRO and site staff is too high and involves redundant work.	Sponsors/CROs want to ensure sites are qualified and have all documentation to show that sites were thoroughly evaluated.	Sites and CROs waste time and resources on redundant meetings.	Sponsors/CROs should prioritize key PSV deliverables and work to reduce the meeting burden on sites by not repeating questions asked earlier in the feasibility process. Leveraging accurate site profile information could support this best practice.

The best practices identified in Table 1 can be distilled into a checklist of minimum necessary documents required before Sponsors/CROs begin the Protocol-specific Site Feasibility process (Table 2). Before any party begins the process, these critical path items should be available. For sponsors, this will reduce inaccurate site responses, and for sites this will result in a more efficient process later during site startup. For all parties, this will result in the least risk and the most optimal outcome. Although it might delay the beginning of the site selection and feasibility process, the reduction in rework and delays later will benefit all parties.

Note that at some sites that have research oversight committees or scientific review committees, it may be better to start the protocol-specific feasibility process before all these documents are available since that process can add up to a month to the process. Knowing site profile information would allow a sponsor to recognize when this might be the case and deviate from this recommendation with a better outcome.

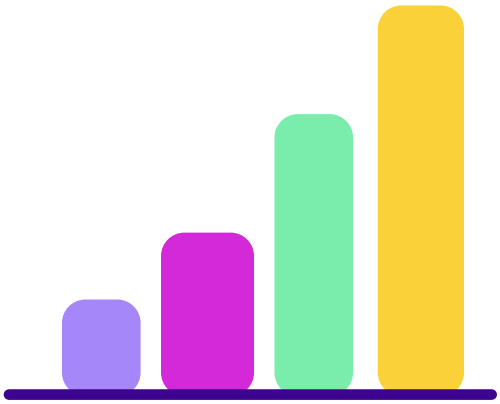
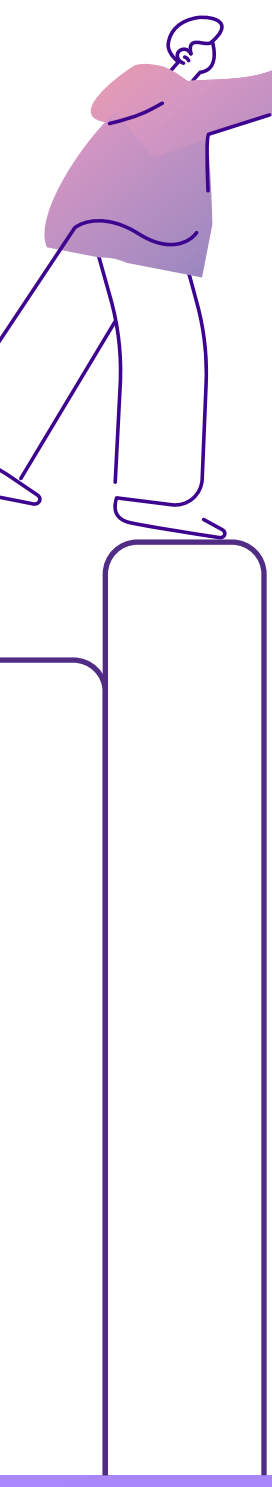


Table 2.

List of Required Materials to Initiate Protocol-Specific Site Feasibility



Documents

Status	Material
☑	Finalized Protocol
☐	Lab Manuals (Draft or Final)
☐	Pharmacy manual (Draft or Final)
☐	Imaging manual / requirements (Draft or Final)
☐	Non-redacted FDA approval letter (for IDE, IND studies)
☐	Finalized CRFs
☐	eCRF completion guidelines
☐	Central lab shipping requirements
☐	Equipment List (Draft or Final)
☐	Budget template (Draft or Final)
☐	Operational manuals
☐	NCT number

Miscellaneous

Status	Material
☐	Pilot/early phase data
☐	Projected timelines for all parties

Table 2:

List of Required Materials to Initiate Protocol-Specific Site Feasibility

Communications

Status	Material
☐	Site Point of Contact Email & Phone Number
☐	Sponsor Point of Contact Email & Phone Number
☐	CRO Point of Contact Email & Phone Number
☐	Communication Plan

Tools Disclosed

Status	Material
☐	List of all vendors and systems being used
☐	EDC
☐	Regulatory
☐	Source
☐	Recruitment
☐	Consent
☐	Inventory Management
☐	Other: _____

Guide for Sponsors/CROs:

1. Engage sites in protocol optimization conversations with early stakeholder engagement meetings and consulting opportunities.

2. Begin Site Feasibility early in the study development process with ONLY the Site Profile and Site Capabilities phases.
   - Use a system that provides up-to-date site data to speed up the process and reduce the site workload.
   - Share within your organization; many times multiple stakeholders from the SAME organization are reaching out to the site asking the same questions.

3. Ensure all critical path items are complete (or drafted) BEFORE starting the protocol-specific assessment phase of Site Feasibility.
   - Refer to the Site Feasibility Checklist provided here (Table 2), or
   - Consider the impact/risk of not including an item, as described in Table 1.
   - Note that final documents are required for sites to accurately assess their ability to meet protocol requirements and for their feasibility assessment to be valid.

Guide for Sites:

Understand and document the steps of your feasibility and start-up processes to allow for consistency and understanding of how the site works. This is useful for internal and external stakeholders.

- [ ] Identify and remove internal bottlenecks wherever possible.
- [ ] Develop a standardized approach which incorporates the tools required to allow for automation and efficiency
- [ ] Understand how this process is impacted by sponsor/CRO processes, since Sponsor/CRO variability does impact site efficiencies.
- [ ] Request and review all sponsor materials when received.
- [ ] Inventory sponsor documents. Immediately request items which are missing, in draft or not in final form from sponsor/CRO.
- [ ] Site standardization for feasibility and startup results in decreased errors and rework due to omissions.

- [ ] Communicate the process and expectations clearly to the Sponsor/CRO.
- [ ] Provide sponsor/CRO with the site process overview when starting the feasibility process. Be clear on expectations and steps of the process.
- [ ] Confirm receipt and understanding of sponsor/CRO expectations and responsibilities in site feasibility and start-up processes.
- [ ] Identify realistic timelines for all steps in the process to give the Sponsor/CRO clarity of what they can expect from the site. Communicate timeline changes real-time, including the reason for any change.

- [ ] Proactively request a meeting with Sponsor/CRO when experiencing difficulty meeting timelines for submissions or negotiations.
- [ ] Promptly respond to Sponsor/CRO requests, especially if it is a reminder that the site is waiting on them to proceed.

- [ ] Rapidly escalate issues to the sponsor when the site feels CRO is being non-responsive; this is equivalent to the sponsor/CRO escalating issues to the PI when there is a concern or delay.

Conclusion

The set of challenges identified by this working group highlight the risks of navigating the feasibility process without considering the impact on all stakeholders. These findings offer a profound opportunity for transformation in the clinical trials industry. The need for enhanced communication, prompt and complete information exchange, standardized procedures, and meaningful collaboration among sponsors, CROs, and sites has never been more apparent. By addressing these issues, the feasibility process can be significantly streamlined, fostering more efficient and successful clinical trials.

It is important to note that this process was explored because of the extreme burden and repetitive work the feasibility process creates for sites.

However, the actual challenges identified have far greater impact on clinical trials than has ever been discussed. The downstream impact on startup timelines and recruitment/enrollment goals is difficult to quantify but clearly meaningful. By bringing awareness and advocating for the industry to remediate these issues now, all stakeholders will benefit. Positive change in this area can result in faster startup times, reduced work, burden and cost for all stakeholders, improved participant recruitment and retention, and improved data quality.

This paper has shed light on a number of emerging issues; however, it is critical to acknowledge that the clinical trials landscape is vast and complex. The specific issues encountered may vary, influenced by factors such as the nature of the trial, the therapeutic area, and the range of stakeholders involved. The working group is aware that not all of these issues will apply in all cases.

To navigate this evolving landscape, industry-wide collaboration and continuous dialogue are vital. By fostering an open, solution-oriented environment, we can leverage the collective knowledge and experience to drive meaningful and lasting change in the clinical trials ecosystem. Our goal is not just to identify problems, but to inspire innovation and proactive improvements that can benefit all parties involved, ultimately accelerating the delivery of critical therapeutics to patients.

We hope that this paper serves as a catalyst for action and invites further discussion on the subject, encouraging the industry to move beyond recognition of the issues and towards the implementation of practical solutions. Through sustained efforts and dedication, we have the potential to shape a future where the feasibility process is not a hurdle, but a facilitator in the pursuit of successful clinical trials.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